The Engineering and Biology of Femoral Impaction Grafting

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Abstract

Femoral impaction grafting is a technique where bone graft is impacted into the femur prior to cementing a stem in place. The technique is designed to compensate for bone stock loss in revision surgery, however it has associated problems of implant movement / subsidence and periprosthetic fractures. The hypothesis for this thesis was that the stability and remodelling of impaction grafting could be improved, either by changing the graft size or by adding a synthetic graft.

To quantify the technique of impaction grafting the Exeter slap hammer was modified, enabling force readings to be measured in nine surgical cases with four different surgeons. The results found that the average force that travels through the impactor is 1.8 to 8.4 kN, which is equivalent to three to eleven times body weight. These readings were used in the subsequent studies to replicate the current technique.

It was hypothesised that varying the graft size might alter the porosity, strength and remodelling of impacted graft. Three graft groups were studied Small, Large and a Graded mix. The results found that the impacted Large graft had higher porosity and lower axial stiffness than the Small and Graded Graft. A noted reduction in graft density was found after six weeks in-vivo compared with twelve, irrespective of graft type. Since density can be related to mechanical strength this led to the question: Could the inclusion of a synthetic bone graft improve the mechanical properties of remodelling graft? A 50:50 mix of allograft and BoneSave™ was compared with allograft. No difference in stiffness was found between the groups after six and twelve weeks remodelling.

These studies were carried out using small test samples either in the laboratory or in-vivo. In order to determine if synthetic graft extenders could be used clinically tests in more realistic models were undertaken. Mechanical analysis was conducted on the 50 % inclusion of two graft extenders with allograft, namely: BoneSave™ and Appapore-60. The results of both projects showed a positive result.

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Chapter 1

Background: Impaction Grafting

1.1 Introduction

Total hip replacements (THR) are one of the major orthopaedic developments of the 20^{th} century. When successful they have the ability to reduce pain significantly and increase function of arthritic hips. Modern hip replacements normally replace the diseased joint with a ball and socket joint; the socket (acetabular cup) is attached into the pelvis and the ball sits at the top of a femoral stem which is driven into the medullary canal of the femur after the femoral head has been removed. The conventional method for fixation of both parts of the prosthesis to the bone is with acrylic bone cement, although screw and press fit fixation of the acetabular cup is common. However, more recently, the development of coatings, surface finishes and custom made CADCAM[1] prostheses has resulted in the use of greater numbers of uncemented hip replacements. Primary hip replacements are extremely successful; the Swedish hip registry quotes success rates of 94.8 % at ten years (Malchau at al, 2002). However as expectations of life quality becomes higher primary hip replacements are being performed on younger patients, and currently there are over 43,000 hip replacements being performed each year in the United Kingdom alone (Hip replacements, 2003). This coupled with an increase in life expectancy has created a situation where many revisions and indeed re-revisions are being performed.

The predominant form of failure of hip replacements is aseptic loosening caused by osteolysis (degeneration and dissolution of the bone). Osteolysis can be a result of the biological reaction to wear debris generated from the ball and socket joint. Wear particles can migrate down the side of the stem, resulting in an area of osteolysis at the distal region of the prosthesis (areas of osteolysis can also be found around the acetabular cup). Osteolysis can also be caused by stress shielding, which is where the stiffer prosthesis shields the bone from the load, consequently areas of unloaded bone resorb. Bone resorption due to stress is usually found in proximal regions. Areas of poor bone quality caused by osteolysis presents a difficult problem at revision, especially as more bone stock can be lost during removal of the old prosthesis and cement. Unfortunately this results in poor clinical survival rates of revised THRs, and limited options for the surgeon.

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[1] CADCAM - Computer added design and manufacture

At revision a custom made prosthesis can be utilized, however this is expensive and the patient will have to wait for the design to be made. A standard prosthesis can be fixed with more cement than the primary. An off-the-shelf long stemmed implant can be used, where the defect in the femur is bypassed and fixation is achieved more distally. The whole joint can be fused. Another option is to rebuild the bone stock by impacting bone chips into the defects before cementing in a new cup or stem. This technique is referred to as "impaction grafting" and because it has the potential to restore bone stock it has received much attention. However, like all revision procedures it is not without problems, stem subsidence and femoral fractures being the most common. Ideally after impaction grafting the bone graft will become revascularised and remodel; this rebuilding of bone stock can increase the life of the prosthesis and if a re-revision were ever to be required it gives the surgeon much more bone stock with which to work.

1.1a Development of Impaction grafting and the Exeter technique

Morsellised bone grafts have long been used in orthopaedics as void fillers. Their use in hip arthroplasty surgery originated in the acetabulum of primary THR for cases with protruded and dysplastic acetabuli (Sloff et al, 1984). In Nijmegen, The Netherlands, Sloff et al (1998) developed the technique of impacting the morsellised bone chips into acetabular defects of both primary and revision THR. During primary THR acetabular defects were filled with morsellised autograft made from the resected femoral head and the posterior iliac crest. Only occasionally were these augmented with allograft. However for revision cases, without the supply of the femoral head autograft, allograft was used, with the occasional addition of iliac crest autograft. All but one of Sloff's 43 cases were pain free and radiographic assessment was encouraging after an average follow up time of two years. In 1985, following Sloffs's success in the acetabulum, surgeons at the Princess Elizabeth Orthopaedic Hospital, Exeter attempted to transfer the technique to the femoral side in revision hip surgery. The surgeons packed morsellised allograft chips into the femur of a patient with gross loss of bone stock, prior to inserting a cement-less long stemmed Exeter prosthesis (Stryker Howmedica). Although the patient's symptoms were relieved and early results looked promising, the prosthesis later migrated distally, so it was decided that the technique should be developed with a cemented stem (Simon et al 1991; Gie et al, 1993a). Following the success at Exeter and Nijmegen, special impaction grafting instruments were made in conjunction with Howmedica (currently Stryker® Howmedica Osteonics[1]): The Exeter X-change® revision instruments.

The developers of the impaction grafting technique give full details of how to use the instruments for the technique (X-change revision instruments, 1998; Gie et al 1993b). For revision acetabular reconstruction the old implant, cement and fibrous interface are removed. Where necessary defects should be closed using wire meshes, which are screwed into place, illustrated in Figure 1.1A. The bone chips are packed into the small cavities, and then layer by layer the entire socket is filled with the graft using different sized, hand held, domed impactors that can be struck with a hammer (Figure 1.1B). The last impactor should be 2 – 4 mm larger than the cup diameter to accommodate the cement used for fixing the cup into position. At least two femoral heads are recommended for acetabular or femoral reconstruction. In the femoral side a bone mill to produce 2 – 4 mm chips is suggested, however larger chips, of approximately 10 mm, are recommended for the acetabulum. These larger chips are produced either by a bone mill or rongeurs. (The variations relating to the graft are in fact far broader than the originators discussed at the time, but will be explored in the Literature Review below).

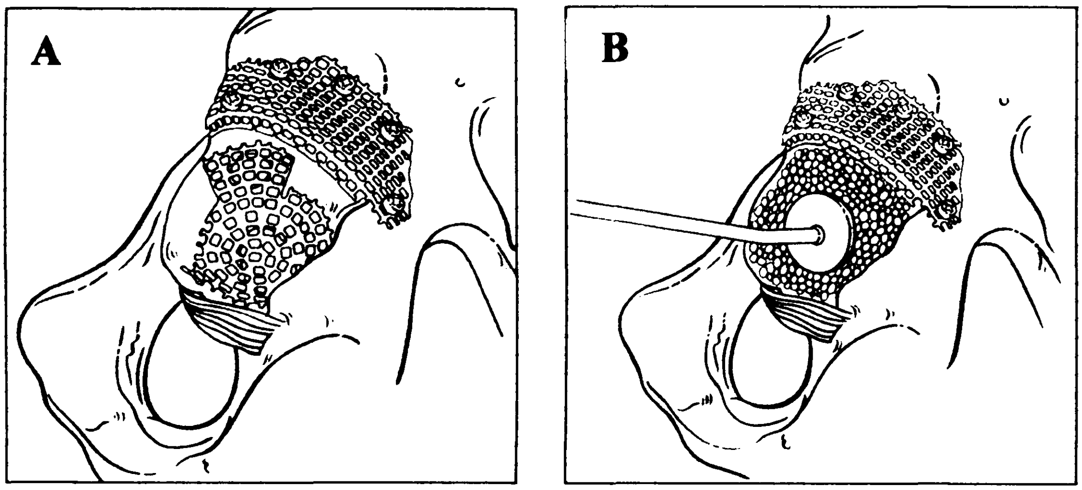

Figure 1.1 - (A) Closing defects using wire meshes, (B) Acetabular impaction (X-change revision instruments, 1998)

On the femoral side the procedure involves first removing the old stem and cement, then any severe cortical defects should be exposed and repaired using stainless steel mesh and cerclage wires. The femoral canal is blocked using a special revision plug

[1] Stryker Europe, Stryker House, Hambridge Road, Newbury, Berkshire RG14 5EG

positioned at least 20 mm distal from the anticipated position of the stem tip, a 4 mm diameter guide wire is screwed into the revision plug, which ensures central compaction of the graft. A series of increasing diameter bulbous rods (distal impactors) that slide over the guide wire, are used to impact the graft distally (Figure 1.2A). To create space for the new Exeter stem a proximal impactor is driven into the graft. The former is of similar shape but marginally larger then the stem to allow for a cement mantle. All distal and proximal impactors attach to a special slap hammer to aid the impaction process. During proximal impaction, graft is added in stages and it is advised that the proximal impactor should be driven into the graft until it is "so tight that it is impossible to withdraw it without using the slap hammer". Once the femur is fully impacted, more chips can be impacted using small hand taps around the top of the stem shaped impactor Figure 1.2B shows proximal impaction and tapping the top layer of graft, after which the new stem can be cemented into place.

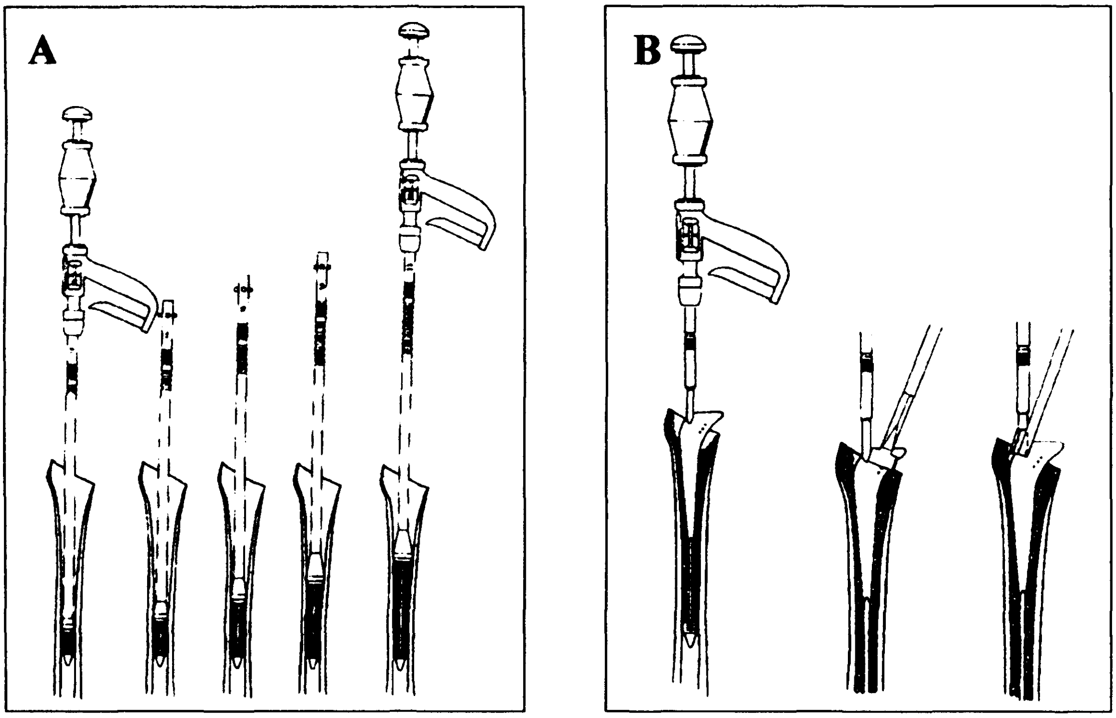

Figure 1.2 - (A) Distal impaction grafting, (B) Proximal impaction grafting and compressing the top layer of graft with small hand taps (Gie et al, 1993b)

The technique for the acetabulum has developed to include uncemented cups. These are usually fixed using screws, which creates space for more graft, and gives better initial stability (Samuelson et al, 1990). On the femoral side the X-change instruments were extended, in 1997, to include impaction of Exeter long stems, which is recommended where there is poor bone stock at the tip of the stem. This can prevent periprosthetic fractures (Halliday et al, 2003; X-change revision instruments, 2001). Other companies have since produced their own impaction grafting kits to match their stems, but to date the Exeter appears the most commonly used in the UK.

The developers of the impaction grafting technique have been able to report encouraging long-term patient outcomes. The follow up by Sloff et al (1998) of 50 hips with acetabular impaction grafting has a 90% survival rate for an average of 11.8 years, with two cases suffering septic loosening (3 and 6 years postoperative) and three cases suffered aseptic loosening (6, 9 and 12 years postoperative). Halliday et al (2003) report 90.5% survivorship at 10 to 11 years for 193 hips with femoral impaction grafting. Many encouraging follow ups have also been published by other users of the technique (Mikhail et al, 1999b; Karrholm et al, 1999; van Biezen et al, 2000; Flugsrud et al, 2000; Boldt et al, 2001; Lind et al, 2002; Gore, 2002; Ullmark et al, 2002b; Pitto et al, 1998; Bolder et al, 2001; Fetzer et al, 2001; Murcia et al; 2001; Schreurs et al, 1998), however there have also been several reports of complications with the technique (Eldridge et al, 1997b; Jazrawi et al, 1999; Meding et al, 1997; Pekkarinen et al, 2000). The predominant forms of failure with acetabular impaction grafting are cup movement and infection; while on the femoral side they are subsidence of the stem, stem rotation, intra-operative and post-operative femoral fractures and infection.

The pressing requirement for a solution to revision surgery, as revision procedures become evermore prevalent, resulted in only limited testing of the impaction grafting technique prior to clinical use. Increasing numbers of THR being carried out and a constant increase in the number of revision procedures addressing problems associated with the fixation of stems in poor bone stock was urgently required. Therefore this technique was developed before full research could be undertaken, and total knowledge and limitations of the technique established. Consequently there have been numerous in-vivo and in-vitro studies, clinical reviews and post-mortems and biopsies performed to help comprehend and improve the technique.

The aim of this thesis was to investigate the hypothesis that the stability and remodelling of impaction grafting could be improved, either by changing the graft size or by adding a synthetic graft.

To enable realist laboratory based studies it was first necessary to evaluate the current surgical technique by recording, intra-operatively the force used to impact the bone chips, by a selection of surgeons. To achieve this the Exeter X-change Impaction system was taken and the hammer developed for force measurements.

The work of this thesis set out to answer the following questions:

- *How variable is the surgeon's technique in femoral impaction grafting?*
- *What is the magnitude of force and energy used in femoral impaction grafting?*
- *Can the bone graft properties be altered to improve the clinical outcome of impaction grafting?*
- *Can the addition of synthetic grafts improve the initial and long term stability of impaction grafting?*
- *What effect on biological incorporation of impacted graft does the addition of synthetic grafts have?*

Fundamentally the research undertaken for this thesis concentrated on the femoral side of impaction grafting, however the findings may well be of relevance to impaction grafting in the acetabulum as the two are interlinked.

Chapter 2

Literature Review

2.1 Background of Bone Grafts

2.1a Bone Formation and Remodelling

At a microscopic level there are to be two prevalent types of bone in an adult human; cortical (dense or compact) and cancellous (trabecular or spongy). Cortical bone forms the casing of all bones, this can vary in thickness depending on the mechanical requirements. Cancellous bone is found in the extremities of long bones and in cuboid bones. Cancellous bone forms a lattice structure orientated to give strength in the direction of loading, and to distribute the stress down the shaft of the bone. The stiffness and strength of bone are strongly correlated with density, hence cortical bone is stronger then cancellous bone. The mechanical properties are also influenced by the strain rate of loading. At strain rates of 10/s the viscous flow of marrow in the bone becomes the predominant factor and significantly increase the ultimate strength and compressive stiffness of bone, however strain rates of 1/s and below have only marginal effects on the mechanical properties. Cancellouse bone has a compressive stiffness of approximately 50 MN/m^2 and an ultimate strength of 6 MN/m^2. Whereas cortical bone has a compressive stiffness of approximately 200 MN/m^2 and an ultimate strength of 17 GN/m^2 (Hayes, 1991,Carter and Hayes 1997).

Cortical bone is anisotropic, at a macroscopic level it comprises of Haversian systems; columns where the orientation is in line with the shaft of the bone. An Haversian system (also known as an Osteon), has a central vascular canal (Haversian Canal) which is surrounded by concentric rings of circumferential lamellae (mineralised bone matrix). Interstitial Lamellae are found between the Osteons. Small cavities, Lacunae, are found along the boundaries of the Lamellae each containing a bone cell (Osteocyte). Cancellous bone is a flat structure of lamellae bone, although not concentric, its consistency is the same as cortical bone, the predominant difference between the two types being density (Cancellous bone density: 5 – 30 %, Cortical bone density: 30 - 90 %). For this reason both cortical and cancellous bone are often referred to as lamellar bone. Bone is a highly active tissue that remodels constantly, in infancy the remodelling of cortical bone in the femoral midshaft may be as high as 50 % per annum, but in a healthy adult this declines to 2 – 5 % per annum. The remodelling is also related to the mechanical environment, if the bone undergoes a period of disuse more bone will be resorbed than new bone laid-down, and vice-versa if the loading is increased. This is generally referred to as Wolff's Law (Wolff, 1892). Remodelling of the bone is a surface event and as such cancellous bone is able to remodel eight times faster than cortical bone. Figure 2-1 illustrates the structure of bone using the shaft of a long bone.

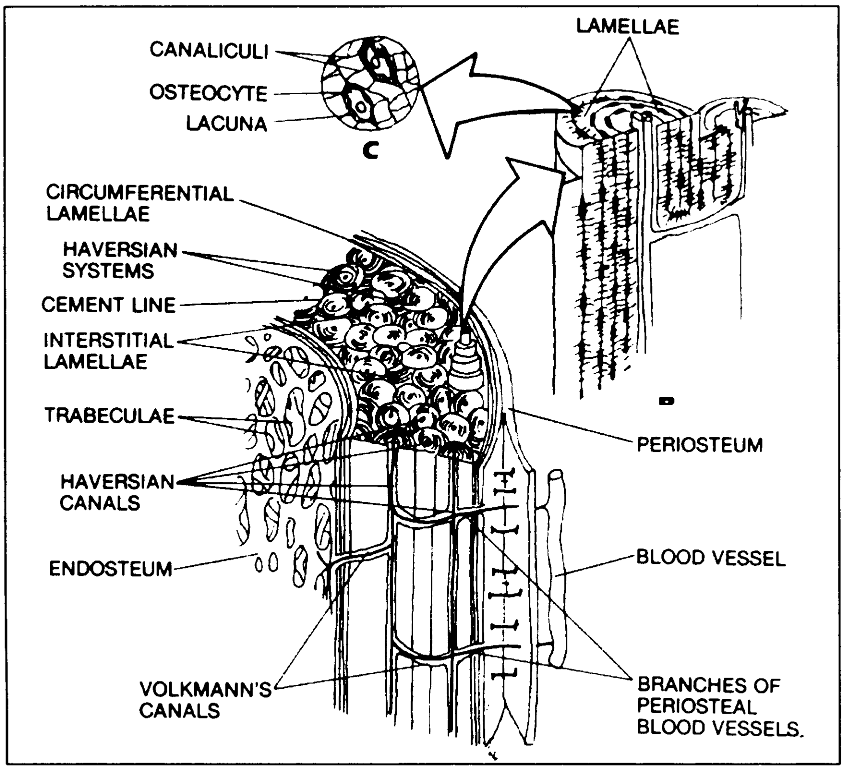

Figure 2-1 - Structure of bone (taken from Nordin and Frankel, 1989)

Remodelling of bone is referred to as Appositional formation and happens within the bone structure, whereas the initial formation of bone is either by Endochondral formation (within the cartilage) or Intramembranous formation (within an organic matrix membrane). Bone resorption is performed by osteoclasts, whilst bone formation is performed by osteoblasts, which often get encompassed into the mineralised bone to form osteocytes. In cortical bone osteoclasts tunnel through the bone, producing a cutting cone, osteoblasts then lay down new bone thereby creating a new Haversian system. In cancellous bone the resorption and formation occurs on the surface of the trabecula. In addition to lamellar bone there is also woven bone, where the collagen fibres have a randomly orientated structure. This bone is found predominantly in foetal bones and replacement with lamella bone commences from one month in age; by four years of age there is little remaining. However woven bone can also be found in healing fractures. After a fracture occurs a hematoma (blood clot) is formed and the site becomes revascularised, this allows a callus to form that consists of fibrous connective tissue, cartilage and woven bone. With time the callus remodels into lamellar bone. (Nordin and Frankel, 1989; Buckwalter et al, 1995; Bostrom et al, 1999).

2.1b Bone Grafts

The use of bone grafts in Orthopaedics is an old and widespread practice. Autogenous graft is tissue that is harvested and used on the same individual; consequently only small quantities are available. Allograft is the donation of tissue to another individual of the same species, hence larger quantities can be obtained. Cortical, non-vascular bone grafts are able to offer good mechanical support but will only be partly incorporated by host bone. Cancellous bone, due to its open structure is capable of becoming totally replaced by the host bone. The incorporation is similar to the fracture repair process, where there is an initial haematoma followed by a fibrovascular response. The dense structure of cortical bone results in high resorption, and loss of mass and strength, prior to new bone formation. In cancellous bone graft this resorption prior to the laying down of new bone is not seen (Friedlaender, 1987), however it is important to remember that even though cortical grafts lose some strength, this is still likely to be superior to cancellous bone. Bulk allografts have been used in revision THR's to reconstruct the acetabulum, however long term follow-ups show high failure rates (Kwong et al, 1993; Hooten et al, 1994). Subsequent post-mortems have shown encapsulation of these bulk grafts by fibrous tissue and only limited evidence of bone union (Hooten et al, 1996).

On the femoral side of revision THR's onlay or strut grafts can be used for segmental cortical defects (Allen et al, 1991; Borja and Mnaymneh, 1985; Head et al, 1999; Head et al, 2000; Oakeshott et al, 1987). Lengths of cortical graft are adhered to the femur using cerclage wires, and it would appear that union of these grafts is successful (Gross et al 1985; Head et al, 1999; Emerson et al, 1990). However the shape of the femur lends itself more easily to the fixation of bulk grafts with cerclage wires, far more than an acetabulum which may be a contributing factor to their success on the femoral side.

The graft itself can contribute to the process of incorporation by osteoconduction and osteoinduction. Osteoconduction is where the graft provides an appropriate open structure for the graft to grow on, i.e. cancellous grafts. Osteoinduction is where stem cells are stimulated to form bone cells usually by the presence of growth factors present in the graft. A number of proteins have been identified which are believed to be involved in this process. The most extensively studied proteins are a group called Bone Morphogenic Proteins or BMPs (Friedlander, 1987). Demineralised bone matrix has good osteoinductivity, however it has poor mechanical strength (Stevenson, 1999) and so is an inappropriate material for impaction grafting. Autogenic graft has some osteoinductive factors, whilst it is debatable whether allograft has any. The body's defence reaction (immune response) to allograft is much higher than with autograft, and varies with immunologic disparities between host and donor. Other factors affecting the remodelling are loading of the graft, stability of the graft, and the vascular supply of the host (Davy, 1999; Stevenson, 1999; Sloff et al, 1998). In a revision operation the vascular supply of the femur is often damaged, which is likely to affect subsequent remodelling.

Morsellised bone grafts (Figure 2.2) have long been used in orthopaedics as non-structural void fillers as they can be compacted to match the shape of the cavity; however their use in revision THR requires structural integrity. The common source of allograft bone, to generate the morsellised chips, are femoral heads obtained during primary THR; these are predominately cancellous bone with a small quantity of cortical bone. The theory behind the impaction of morsellised graft is that the allograft chips will become revascularised and remodel after a period of time, this increases the longevity of the new prosthesis, whilst also giving the surgeon an improved bone stock to work with, should a re-revision ever be required. Morsellised graft does not have the same initial strength as a cortical bone graft, but it is able to withstand compressive loads, and due to its open structure should not resorb significantly during the early stages of remodelling unlike cortical bone grafts (which are known to resorb and lose mechanical strength). Initially surgeons believed that they were able to observe modelling radiographically (Gie et al, 1993a; Eldridge et al, 1997), however many now think that radiographs are misleading and portray an inaccurate picture. In light of this the best way to assess bone regrowth is through histology of specimens taken during post-mortems or from biopsies.

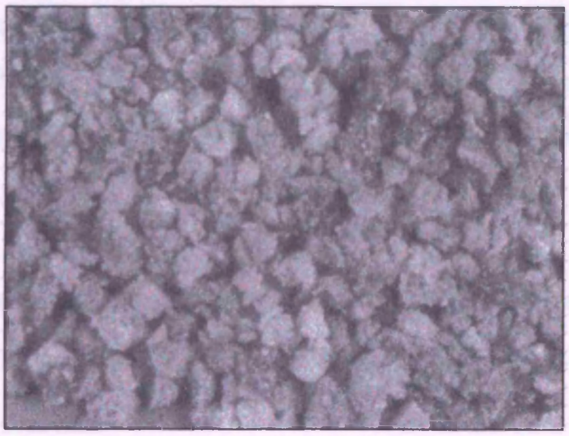

Figure 2.2 - Morsellised bone graft

Heeken et al (1995) performed the post-mortems of retrieved acetabuli 18, 53 and 83 months after impaction grafting without cement. These were able to illustrate the progressive remodelling stages; at 18 months there were still large quantities of the original allograft, which were surrounded by myxofibrous[1] tissue. At the peripheries of the graft there was vascular penetration and in a few of these areas osteoclastic resorption and formation of new bone was visible. At 53 months, small fragments of allograft were surrounded by new bone, osteoblastic and osteoclastic activity was seen and the graft was 90% revascularised. By 83 months the graft had become totally incorporated making it difficult to distinguish the original fragments of allograft. Buma et al (1996) took biopsy from eight patients at re-revision of the acetabuli, again they were able to demonstrate the incorporation process with respect to time. Four biopsies were available to examine the graft cement contact, one of which showed vital bone in direct contact with the cement layer; however, a soft tissue interface predominated. A study of 24 acetabular biopsies from 20 patients (Schreurs et al, 2001) was able to give an even better picture of incorporation. At three months there was already some incorporation, at four and five months a vascular form was visible, with osteoclasts removing bone and osteoblasts forming osteoid (uncalcified bone matrix) and woven bone. At eight and nine months the graft was embedded in the new trabecular structure. The bone closest to the graft-cement interface contained mostly woven bone, because the revascularisation and remodelling front arrived latter at this location. The later biopsies showed normal trabecular bone, without traces of woven bone. The graft in all these studies were fresh frozen femoral heads, it is presumed they are not washed as no references were made to this.

An in-vivo study in goats (Schimmel et al; 1998) was able to show virtually complete incorporation of the graft around the acetabulum by 12 weeks. However a soft tissue interface grew between the graft and cement resulting in loosening in the majority of cups by 48 weeks. Unfortunately no clear picture emerged as to why there was such discrepancy in the speed of remodelling and formation of the detrimental fibrous interface.

There have also been several studies on the histology of femoral impaction grafting; Ling et al (1993) assess a retrieved femur 3.5 years postoperative, Neilsson et al (1995)

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[1] myxo- forms indicating association with mucus (Dictionary of medical terms; 2000)

analysed four biopsies 11 to 27 month after surgery, Ullmark and Linder (1998) discuss a retrieved femur 6 months post operative, Mikhail et al (1999a) performed a biopsy 27 months post-operative (Figure 2.3) and Linder (2000) undertook six autopsies and eight biopsies three months to eight years after impaction grafting surgery. These results for the femur all have similar findings but the incorporation process seems varied and inferior to the incorporation observed in the acetabulum. The above studies identified three relatively undefined zones: an inner zone consisting of bone cement, fibrous tissue, partially necrotic bone and some evidence of bone remodelling; a middle zone consisting of viable trabecular bone with few particles of bone cement; and an outer zone consisting of viable cortical bone. Both Linder (2000) and Mikhail et al (1999a) were able to find some cases were mineralised bone was in contact with the cement, and indeed in some case Linder (2000) noted this osteoid/ bone formation reaching up to the implant. However all the papers discuss the fibrous tissue that envelopes the graft particles. Linder (2000) believe that this dense fibrous tissue originates as a cell-rich mesenchymal[1] stroma and goes on to discuss that although the tissue may be replaced by bone, for many patients elements of this fibrous tissue could remain indefinitely. Figure 2.4 illustrates work from Nelissen et al (1995) showing a necrotic piece of bone surrounded by viable new bone.

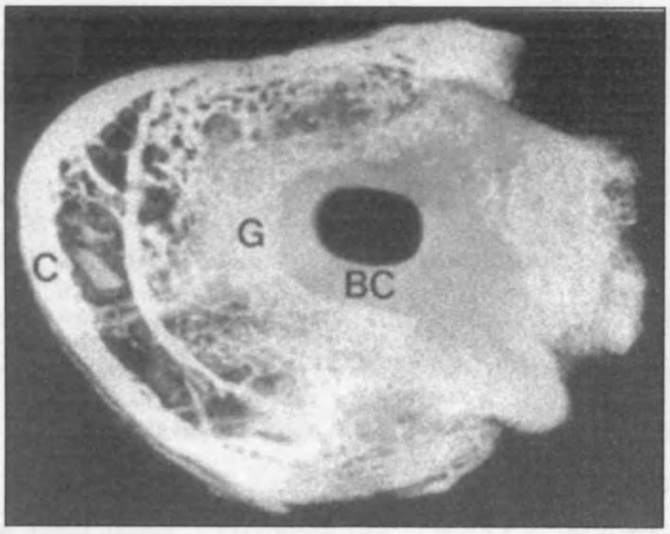

Figure 2.3 - Radiograph of femora biopsy section (Mikhail et al, 1999a), shows cortex (C), graft (G) and bone cement (BC)

[1] Mesenchyme – embryonic tissue that forms connective tissue, blood and smooth muscles

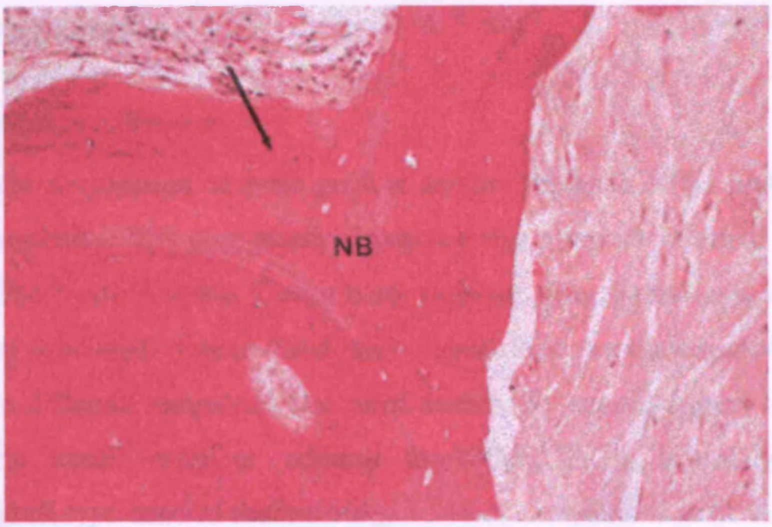

Figure 2.4 – Fragment of necrotic bone (NB) surrounded by areas of viable new bone (arrow), (Nelissen et al, 1995)

There are many that would argue that the composite of fibrous tissue and necrotic bone granules give adequate long term clinical stability (Linder, 2000; Ullmark and Obrandt, 1999; Aspenberg, 2001, Mikhail et al, 1999a); and indeed Tagil and Aspenberg (2001), in a bone chamber study in rats, proved that the mechanical strength of bone chips doubled after four weeks of fibrous tissue ingrowth. Another finding from the above histological studies was the disparity between the radiographic interpretation and histology; in particular a lack of radiolucent lines does not necessarily indicate absence of soft tissue, which would be the natural interpretation.

Schreurs et al (1994) performed experiments in goats and were able to conduct loading tests, which resulted in some axial rotation and subsidence of the prosthesis, which showed some elastic recovery after removal of the load. Their findings were that an improvement in stability can be noted at 6 weeks, but that the integration process was not complete by 12 weeks. A histological study backed these findings and showed that the progress is faster proximally than distally, which they attribute to vascular disturbances in the distal cortex. However, out of the 14 goats used in the study, there was one aseptic loosening with gross movement.

2.2 Graft preparation

2.2a Storage and Sterilisation

The storage and sterilisation of bone graft is another factor to effect its biological and mechanical properties. It is now standard practice that allograft is stored at specialized bone banks. The North London Tissue bank supplies several products; fresh frozen (-70^{0}C), frozen irradiated, freeze-dried and freeze-dried irradiated graft to suit the demands from different surgeons. The most commonly supplied graft is whole fresh frozen femoral heads, with or without irradiation. Fresh frozen graft was the predominant graft type used in the histology cases of morsellised graft discussed above (Section 2.1b), however there was no reference as to whether it had been irradiated. The Tissue banks can also supply, at a premium, the graft pre-morsellised (which includes removal of soft tissue and cartilage, plus a washing step to defat the graft). As already mentioned the standard source of allograft to create morsellised bone chips is femoral heads saved from primary THR. Consequently they are retrieved aseptically, and are normally microbial contamination is determined at the time of collection, in addition it is a requirement that the donors are tested for markers of virus and disease transmission on two occasions at least 6 months apart before the tissue can be released (Blood matters, 2001; British Association for Tissue Banking, 1999). Additional sterilisation is precautionary for most of the bone grafts and only a necessity when bacteriology tests are positive.

Freezing of the graft reduces the immunologic response, but does not greatly affect the mechanical properties (Boyce et al, 1999). Freeze drying the graft reduces the moisture content to less than 6 %, enabling storage up to five years at room temperature (British Association for Tissue Banking, 1999). This also reduces the immunologic response, but it believed to have detrimental affects on the mechanical properties, particularly when the graft has been irradiated (Boyce et al, 1999; Davy, 1999, Pelker et al, 1983). However Cornu et al (2001) did a compaction study of morsellised freeze-dried and fresh frozen graft. The results actually found that initially they had similar stiffness but after 3, 10 and 50 impactions the freeze-dried graft had higher stiffness, however after 150 impactions the stiffness of the two graft types was similar. The fresh frozen graft had not been defatted which probably contributed to these findings. Heiple et al (1963) performed a large study of graft types in dogs, and rated the freeze-dried allograft second only to fresh autograft and better than frozen allograft. However freeze-dried, irradiated allograft was rated bellow frozen allograft and frozen irradiated allograft. Fresh frozen allograft is the more commonly used graft for impaction grafting procedures, consequently there are only a limited number of short and mid-term follow up reports on impaction grafting with freeze-dried graft (Thien et al, 2001; de Roeck and Drabu, 2001; Williams et al, 1998; Mazhar Tokgozoglu et al, 2000). de Roeck and Drabu (2001) reported on a series of 32 patients undergoing impaction grafting with freeze-dried grafts, the survival rate was 91 % at four years. They discussed the necessity for prolonged rehydration of the graft prior to impaction and stated their preference of using fresh frozen graft with regards to its handling. Thien at al, 2001, also stated a preference of fresh frozen graft and only used the freeze-dried graft when no fresh frozen graft was available. With an average of seven years follow up the survival rate was 86%, which they describe as satisfactory, but refer to the lack of histological evidence to prove graft remodelling and incorporation. However Mazhar Tokgozoglu et al (2000) used scintigraphic examination, after an average of 14 months, to demonstrate that the area corresponding to the allograft had a remarkable accumulation of radioactivity accumulation which the believed to indicate new bone formation, although this technique for monitoring incorporation is not highly regarded (Nelissen et al, 1995). Unfortunately no accounts of histological examination of freeze-dried morsellised allograft could be traced.

As mentioned above irradiation can have detrimental affects on the graft, however irradiation below 20 kGy does not dramatically alter the mechanical properties of frozen allograft and is effective at killing bacteria. To kill viruses a dose greater than 30 kGy is required, but unfortunately this is known to affect the mechanical properties of the graft (Stevenson, 1999). The standard dose administered by UK bone banks is 30.3 kGy (NLTB, 2002). Another method of sterilisation is ethylene oxide, which does not affect the mechanical properties of the graft (Davy, 1999) but impairs the bone conductive properties of fresh frozen bone grafts (Aspenberg and Lindqvist; 1998). The residuals left after ethylene treatment are inflammatory and therefore this method of sterilisation is less commonly used for musculoskeletal grafts (Stevenson, 1999).

There have only been a few radiographic follow up cases specific to the use of irradiated bone in impaction grafting (Robinson et al, 2002; Holt et al, 2001). In the acetabulum there appears to be no difference in incorporation and remodelling after six and 12 months (Holt et al, 2001). Robinson et al (2002) are more sceptical, with an average follow up of 27 months for 57 hips they found 34 % cortical repair, 39 % graft incorporation but no trabecular remodelling. However their concerns seem to lie with the lack of trabecular remodelling rather than the cases of failures, which they believed to be common with other studies. Radiographs are not always an accurate representation, but perhaps the irradiated graft is acting in the manner described by Linder (2000); engulfed in fibrous tissue but still providing adequate structural support.

2.2b Washing of the graft.

The pre-morsellised graft supplied by the North London Tissue banks is washed, the washing process takes several hours and includes ultrasonic washing to remove cells and blood plus an ethanol wash to denature cellular proteins. This process also kills some viruses and bacteria (North London Tissue Bank, personal communication; Stevenson 1999). Washed allograft has reduced immunogenicity, and so superior incorporation, conversely washing of autograft reduces its osteoinducivity and hence incorporation, consequently there is no difference in the remodelling of washed allograft and autograft (Thorén et al, 1995; van der Donk et al, 2003). Moreau et al (2000) also advocated a defatting procedure, especially prior to gamma irradiation; they found irradiating non-defatted graft induced lipid peroxidation, which they believed to invoke cell death. Dunlop at al (2003) proved that washing morsellised graft in normal saline using a pulse-lavage gun increased its resistance to shear. Voor et al (2000) investigated the grafts mechanical properties using compaction and consolidation tests and looked specifically at the water and fat content. Reducing the moisture content of the graft resulted in higher compaction and reduced strain under consolidation. Reducing the fat content improved the properties further. Unfortunately washing of the graft is not common practice, consequently the histology cases with fresh frozen graft reviewed in section 2.1b were not from graft which had been defatted, and indeed nor were the follow up cases of irradiated frozen graft by Robinson et al (2002) and Holt et al (2001).

2.3 Clinical practice

As already mentioned in the introduction the published clinical outcomes vary in their success rates. However most of the papers that write favourably about the outcome using impaction grafting in the femur still have failures relating to stem movement, and often the cases that are considered successful also have noted subsidence (Halliday et al; 2003; Mikhail et al, 1999b; Karrholm et al, 1999; van Biezen et al, 2000; Flugsrud et al, 2000; Boldt et al, 2001; Lind et al, 2002; Gore, 2002; Ullmark et al, 2002b; Fetzer et al, 2001; Murcia et al; 2001). Since stem movement is such a problem what are its probable causes and how can it be reduced? The most obvious reason for stem subsidence in an unfractured femur could be the sinking of the stem into the cement, settling of the bone chips, resorption of the bone chips or subsidence of the distal plug with progressive subsidence of the rest of the structure.

The team at Exeter who developed femoral impaction grafting used the Exeter stem; a double tapered, collarless polished prosthesis. Fundamentally there are two schools of thought on primary cemented prosthesis design; the self tightening polished wedge style, such as the Exeter, which is intended to subside into the cement; or rigid fixation into the cement using a stem with a collar and rough surface finish, the Charnley[1] and the Stanmore[2] are the most longstanding examples. Figure 2.5 illustrates the Charnley, Stanmore and Exeter femoral components. For a long time the Charnley was considered the gold standard of hip replacements, developed in the early 1960's it has over thirty years of clinical follow-ups, however minor tweaks were constantly made to the design and the stem produced by DePuy today is no longer a replica of the original Charnley stem. Also introduced in the Sixties, the Stanmore stem has maintained its original geometry, material and surface finish. (Which design of hip replacement, 2003). Although not an original concept for the design choice of the Exeter stem when it was invented in 1969 (The double taper, 2003), the double taper is said to subside into the cement, enabled by the cements viscoelastic properties, and does not attempt to create a bond between the cement stem interface, hence the polished surface finish (Spitzer, 2001). Consequently the axial loading forces are converted into radial compressive forces (hoop stresses), which maintain the bone quality for the long term (Shen, 1998).

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[1] Charnley hip – DePuy Leeds UK

[2] Stanmore hip – Biomet Merck Swindon, UK

Another example of collarless polished taper design style is the CPT[1]. Small subsidence is found in primary cemented stems of this design in clinically successful cases (Fowler et al, 1988) and Kärrholm et al (2000) found that in primary interventions the Exeter migrates axially within the cement more than any other style of prosthesis.

When a rough surface finish is used the interlock between the cement and implant is superior, however with time it has a higher chance of generating wear debris, so is unstable for the taper slip design. The collared stem design was intended to minimise subsidence and to transfer maximum proximal loading. Unfortunately the two different philosophies were not always understood and in the mid seventies the Exeter stem was used with a matt surface finish, which produced catastrophic results (Ling, 1997). For impaction grafting the basic concepts of primary cemented hips remains, the only notable difference is the use of long stems to bypass distal defects.

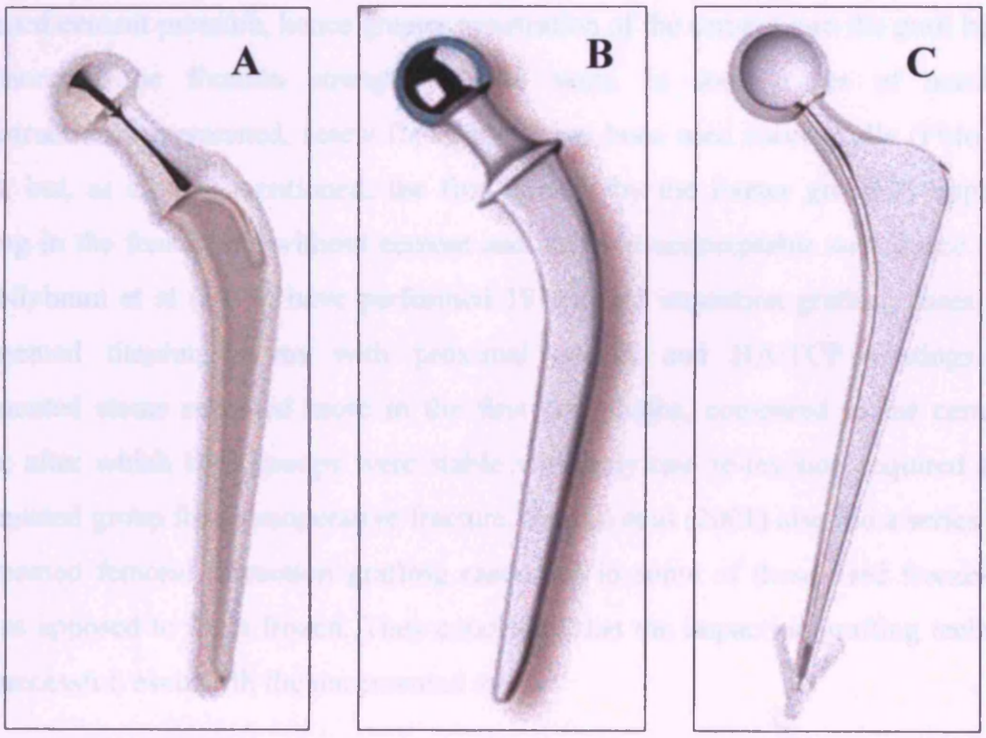

Figure 2.5 - (A) Charnley hip (B) Stanmore hip (C) Exeter hip

Masterson and his colleagues in Vancouver, Canada, express concern about the cement mantle in impaction grafting cases and are of the opinion that this could be a

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[1] Zimmer, Warsaw, Indiana, USA

contributing factor to subsidence (Masterson et al, 1997a; Masterson et al, 1997b; Masterson et al, 1999). The Vancouver group were able to show incidences of cement fractures and cement voids in cases of progressive subsidence with the Exeter stem. They went on to examine the cement mantle (which fundamentally is the size difference between the proximal impactor and the stem) with the Exeter, CPT and Harris[1] impaction grafting systems and expressed concern with regard to the completeness of the cement mantle produced with the Exeter system. Nelissen et al (2002) were also able to show cases of subsidence with cement mantel defects using the Exeter system by Radiostereometric analysis (RSA). Radiostereometric analysis is where tantalum markers, normally small beads, are inserted into the bone and cement at the time of operation, and are also attached to the prosthesis; the movement of these markers can be monitored by radiographs enabling a clear picture to emerge of the relative movements of prosthesis, bone and cement (Selvik, 1989; Kärrholm et al, 1997).

However, in an in-vitro mechanical experiment Berzins et al (1996) proved that increased cement pressure, hence greater penetration of the cement into the graft bed did not increase the fixation strength of the stem. In some cases of acetabular reconstruction, uncemented, screw fixed cups have been used successfully (Pitto et al, 1998), but, as already mentioned, the first attempt by the Exeter group at impaction grafting in the femur was without cement and suffered unacceptable subsidence. Since then Nivbrant et al (1999) have performed 19 femoral impaction grafting cases using uncemented titanium stems with proximal porous and HA/TCP coatings. The uncemented stems subsided more in the first six months, compared to the cemented group, after which both groups were stable with only one re-revision required in the uncemented group for a preoperative fracture. Santori et al (2001) also did a series of 23 uncemented femoral impaction grafting cases and in some of these used freeze-dried graft as apposed to fresh frozen. They concluded that the impaction grafting technique was successful, even with the uncemented stems.

Schreurs et al (1991) performed a time zero comparison of cemented and uncemented femoral impaction grafting. They used sheep femurs as a model and performed mechanical testing of the implants. Unfortunately the rotation of the cemented stems was approximately four times lower than the uncemented stems. However it is possible

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[1] Zimmer, Warsaw, Indiana, USA

that cementing with impaction grafting can compensate for poor initial graft compaction and that results would have looked different with higher initial impaction. The researchers then went on to perform an in-vitro mechanical stability experiment of uncemented hydroxyapatite (HA) coated stems, with impaction grafting, in 14 goat femurs (Schreurs et al, 1996). Despite height failure rates (two loosening and two fractures of the eight specimens intended for mechanical testing), the stability at 12 weeks was greatly improved from the previous time zero study. The histology showed revascularisation and bony ingrowth, particularly in the proximal lateral area. Unfortunately a cemented impaction grafting was not conduced as a control.

Currently few surgeons would see a necessity for using uncemented stems with impaction grafting, as any possible benefits are outweighed by the increased failure risks. However with time, once the impaction process has been fully developed and standardised it may be possible for more research to be undertaken on uncemented stem design for impaction grafting. The stem will probably require a series of grooves running down the graft to interlock with the graft, as well as HA coating. However, realistically its use would be limited to cases with only minor defects and young patients where re-revisions are more likely.

Returning to the issue of stem design and surface finish of cemented stems; van Doorn et al (2002) conducted a follow-up comparison of the Exeter and Elite Plus[1] (matt-surfaced flange collared) stems using RSA. As one would expect they found considerably more overall subsidence in the Exeter group. However the movement of the Elite Plus was different, with greater medial and posterior migration of the femoral head. After two years the radiographs did not highlight any additional effect on the remodelling around the Exeter stems. However the benefits of the radial hoop stresses supposedly generated with the tapered design may be more long term than the researchers realised. A follow-up study of impaction grafting cases by Ullmark et al (2002a) looks at two different types of hip design; the Lubinus (Waldermar Link GmbH & Co, Germany) wide collared, double curved matt finished stem and the Charnley (DePuy, Leeds) matt surface, narrow collared stem). Of the 47 cases there was early minor subsidence in a few cases, two reports of progressive subsidence requiring re-revision, some intra operative fractures and four postoperative fractures. The patient

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[1] Johnson & Johnson, Haarlem, The Netherlands

outcome was similar between the groups although only one of the postoperative fractures was with the Lubinus stem, which they attributed to the longer length of this stem compared with the Charnley. Remodelling was observed through radiographs, biopsies and one autopsy. This does not appear to contrast from findings with other stem design, although radiographically more trabecular remodelling was observed in the Lubinus group. Interestingly the fresh frozen graft used in this series was rinsed in warm saline to remove most of the fat. This should automatically improve the mechanical properties of the graft and graft incorporation, which may contribute to the success of this study. Other studies have also used collared stems resulting in positive clinical findings (Boldt et al, 2001; Franzén et al, 1995; Masterson et al, 1999, Kärrholm et al, 1999). Voor et al (1998) performed a study in a goat model to compare a polished and grit blasted stem. They found that the surface finish did not effect the histology or mechanical stability. Most of these studies conclude that prosthesis design is not a major factor for long term success but that that the surgical technique and graft preparation is (Boldt et al, 2001; Franzén et al, 1995, Voor et al, 1998).

Another supposed advantage of the double tapered style stems is their proximal loading of the femur, which should encourage bone turnover (Fowler et al, 1988). However van der Donk et al (2000) performed an experiment using a subcutaneous pressure implant to examine the effect of load on graft incorporation. They did not find significant differences between the loaded and unloaded grafts, but did not rule out the effect of low level physiological loading on the unloaded graft obscuring a difference. Wang et al (2000), in a tibial tray study in rabbits, also examined the effect of load on graft remodelling and found new bone formation and resorption of the graft were increased in the loaded grafts, and concluded that load increases the rate or speed of remodelling.

Stulberg (2002) reports a variation of the technique, which they refer to as radial impaction grafting (RIG). The notable difference in the technique appears to be radial impaction with a conical proximal impaction prior to a prosthesis profile impaction. Unfortunately the geometry of the prosthesis is not described, and follow-up is only for 14 patients and relatively short (five to seven years). They boast the use of long stems apparently unaware that the Exeter X-change instruments were updated to include long stems back in 1997. Although their results are encouraging, there is little discussion on the difference from the current technique.

2.3a Surgical Technique

Many of the papers reviewed so far have discussed the importance of the surgical technique, however it appears to still be an unquantified variable. As well as subsidence, another common problem with femoral impaction allografting is periprosthetic fractures. These are common during surgery as well as post-operatively. It is interesting to note that in the Exeter series (Halliday et al, 2003) intra- and post-operative fractures caused a greater number of re-revisions in their series, than subsidence. **Is this any reflection on their technique, higher initial impaction of the graft preventing later subsidence but causing these fractures instead?** However Holliday et al (2003) mention that the use of long stems substantially reduced the occurrence of post-operative fractures in their series.

It is also possible that femoral fractures are associated with the initial bone stock of the femur prior to revision. Some surgeons chose to save impaction grafting for cases with severe loss of femoral bone stock (Leopold et al, 1999; Masterson et al 1997a; Meding et al, 1997) and possibly as a consequence have high rates of femoral fractures and femoral perforations. In order to compare results from different studies it is necessary to perform pre-operative assessment of the initial femoral bone stock, which can be conducted using a number of classification systems. These include; Chandler and Penenberg, Endo-Klinik, Engh and Glassman, Paprosky et al., Mallory, Gross et al., Johnston et al., Gustilo and Pasternak, and American Academy of Orthopaedic Surgeons Committee on the Hip (AAOS), all of which are described by Haddad et al (1999). Haddad et al (1999) conducted an assessment comparing the AAOS, Paprosky et al and Mallory classification systems. The results found little difference between the systems, with only moderate intra observer agreement and slight inter observer agreement for all three classifications. The authors concluded that the AAOS is the most comprehensive and most consistently used.

There are two basic categories of the AAOS femoral bone loss classification system (D'Antonio et al, 1993), which are Segmental (I) and Cavitary (II), the full list of categories is listed in Table 2.1. Segmental deficiencies may be Proximal (partial or complete), Intercalary or Greater Trocenteric. Whereas Cavitary defects can be referred to as Cancellous, Cortical or Ectasia, Ectasia refers to an enlarged medullary canal.

Category	Description
I	Segmental deficiencies Proximal Partial (anterior, medial or posterior) Complete Intercalary Greater Trocenteric
II	Cavitary deficiencies Cancellous Cortical Ectasia
III	Combined Segmental and Cavitary
IV	Malalignment Rotational Angular
V	Femoral Stenosis
VI	Femoral Discontinuity

Table 2.1 – Definitions of AAOS Femoral Bone Loss Classification System

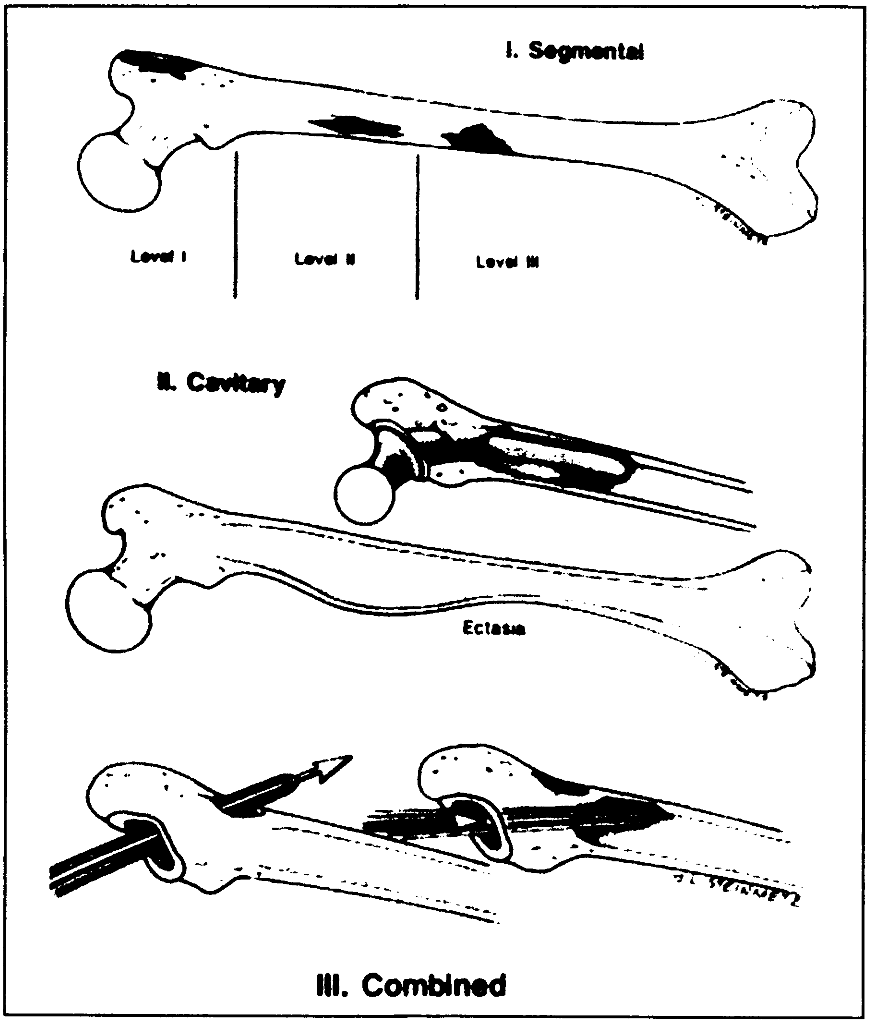

Figure 2.6 - AAOS Classification system: (I.) Segmental, (II.) Cavity, (III.) Combined (taken from D'Antonio et al, 1993)

Another study to throw up variation in surgical technique was a mechanical comparison of small and large graft particles in an acetabular model (Verdonschot et al 1999). Two surgeons conducted the experiment and the migration results with the large graft were similar for each surgeon. However for Surgeon A the small graft resulted in substantial subsidence, but with Surgeon B the subsidence was similar, if not better, with the small graft compared to the large. They concluded that the solution to variations in surgical technique is to use larger graft particles. So quantifying the technique seems a necessity to the unravelling of the success and failures of impaction grafting. **What are the magnitudes of the forces currently used in surgery? How many impactions, and quantity of energy, are used to impact the graft? How much may this vary for a given surgeon between cases? How variable is the technique between surgeons and centres?**

Hostner et al, 1997, tried to reduce this surgical variation by impacting the graft using an air powered machine attached to the phantom prosthetic, the frequency was 60 Hz and amplitude was 2.5 mm. Unfortunately the results were poor, with higher migration and more varus migration than in the control group where the standard impaction procedure had been performed.

Another aspect of impaction allografting that is determined, in part, by the surgeon is post operative load bearing (although the patient may not choose to follow the surgeons recommendations). The initial recommendations of Gie et al (1993b) were three weeks bed rest followed by three months of only touch weight bearing before the gentle reintroduction of weight bearing. However, Ornstein et al (2003) compared the migration of a group of patients mobilized with unrestricted weight bearing with a group who had had restricted weight bearing for the first three months, this was measured using RSA. They found no increase in migration in the group allowed to freely weight bear compared with the restricted weightbearing group. However only patients without intra-operative complications were used in the unrestricted group. They concluded that when the femoral bone feels competent, patients should be allowed to weight bear as this simplifies mobilisation and might enhance graft remodelling.

2.4 Graft Properties

One way of assessing the subsidence in impaction grafting is by using radiosterometric analysis (RSA) with marker beads. Ornstein et al (1999) used this to find that the cement mantle migrated in relation to the femur by approximately 0.3 mm in the first three months (the stem relative to the cement subsided approximately 1.8 mm in the first three months), which one assumes is compaction of the graft bed. Since it is evident that the graft is contributing to the subsidence observed in impaction grafting cases, numerous studies have been undertaken to quantify the mechanical properties of the graft at various stages of compaction.

Morsellised graft is in essence a particulate material and as such can be analysed using soil mechanics theory. Brodt et al (1998) were one of the first to characterise the properties of particulate graft, to do this they performed triaxial compression tests at different confining pressures. The load deformation curves of the graft exhibited two nearly linear regions which they describe as the pre-crush and crush regimes. They postulate that the projected trabeculae of the particles allow for interlocking, however as the loading increases these break allowing the morsels to slide relative to one another. They concluded that the uncrushed graft had a Young's modulus of approximately 100 MPa. Another aspect Brodt et al (1998) investigated was the effect of particle size. The morsellised graft was produced using a Tracer Bone mill[1], which produced a broad distribution of weight fraction as a function of graft size. Triaxial measurements were performed on samples from three size ranges (less than 0.53 mm, 0.53 - 1.14 mm and 1.52 - 2.46 mm). The results showed that this did not greatly affect the mechanical properties.

A surgical bone mill is the easiest way of producing the morsellised graft, the rotating rasp bone mill is the most common design although the reciprocating blade is also used. The rotating rasp is like a large cheese grater and produces very flaky chips, the size of which depends on the rasp used. They can be operated by hand or driven pneumatically. Some examples of this mill type are: Tracer, Bull, Howex, Novomgus and Norfolk. The most frequently used reciprocating blade style is the Lere Bone mill[2], a toothed blade is

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[1] Tracer bone mill –Tracer Designs, Santa Paula, CA, USA.

[2] DePuy, Warsaw, USA

driven across the bone by a pneumatic punch and it has been found to produce chips of a larger size, broader size distribution and with stronger mechanical properties than those produced with the Tracer rotating rasp (Tanabe et al, 1999).

The size distribution of the graft (grading) has been discussed and its relationship to soil mechanics (Brewster at al; 1999). The resistance of a particulate mixture from shear failure is a function of interlocking of the particles and frictional resistance. Grading the particles in a mix will reduce its resistance to shear, by increasing the frictional resistance. Brewster et al (1999) proved the theory of grading by adding the necessary quantities of bioglass particles (that had inferior shear strength to the bone chips) to the bone chips to match the optimal curve for irregular shaped particles. However since the grading of the particles maximises density, they expressed a view that "in a well-compacted, well-graded, allograft aggregate, revascularisation and re-incorporation may be inhibited by the close packing of the graft." If this opinion is correct, it would pose an even greater problem to the surgeon: namely to impact well enough to prevent minimal subsidence of the implant without over packing, thereby preventing revascularisation and re-incorporation.

Tagil et al (1998) looked at the effect of impaction on the remodelling rate of the graft. The study was performed in titanium bone chambers screwed onto the rats tibias bilaterally. On one side graft was compressed into the chamber with either 25 or 2500 MPa, on the other an uncompressed graft was used as a control. The results found more bone ingrowth into the un-compacted controls compared with the impacted grafts, and higher tissue ingrowth into the graft compacted with 25 MPa compared to 2500 MPa. Although the authors were surprised by their findings it is important to note that the graft was not subjected to any levels of physiological loading, a natural stimulus for remodelling. Also the grafts had not been washed which is another factor that may have inhibited the remodelling of the bone. However the findings of Tagil et al (1998) may support the point by Brewster et al (1999) that grading the graft will inhibit remodelling.

Griffon et al (2001) used the theory of grading the samples for an in-vivo ovine study in a bone defect model. Unfortunately they were comparing the graded allograft samples with graded mixes of bioactive glass and tricalcium phosphate-hydroxyapatite so no comparison could be produced with respect to remodelling of an upgraded sample.

Therefore it would appear that the question remains as to the incorporation rate of a sample produced from a broad range versus a narrow range of particles size?

Studies have shown that the initial compaction of morsellised graft improves its compressive stiffness (Tanabe et al, 1999), increases the mechanical strength in shear (Brewester et al, 1999) and minimises subsidence (Ullmark and Nilsson, 1999). The morsellised graft particles can be described as an elasto-viscoplastic material. Consequently preconditioning of specimens produces large, irreversible deformations, which are caused by the flow-independent creep behaviour (Giesen et al; 1999). The design of the proximal impactors and the prosthesis must take into account the elasto-viscoplastic properties of the graft. The proximal impactor must accommodate for the recoil of the graft after impaction to ensure an adequate cement mantel (Ullmark and Nilsson; 1999) and the prosthesis must accommodate, without loosening, any permanent deformation caused by compressive weight bearing (Giesen et al; 1999).

Ullmark and Nilsson (1999) found less subsidence with bigger chips which agrees with the findings of Vendonshot et al (1999) who found that large graft gave more consistent results for time zero mechanical tests (as already discussed 2.3a Surgical Technique). ***However if large graft is superior for mechanical properties, is there a difference in the remodelling rate compared with small graft?*** Small graft will have a higher exposed surface area, however it will have small spacing for vascular penetration.

As already stated, the common form of allograft is femoral head and it is common in the UK to remove the cartilage and any remaining soft tissue prior to morsellising in a bone mill. Experiments by Bavadekar at al (2001) found that if the cartilage was removed prior to milling, the stiffness of the graft was increased. They also showed that inclusion of the femoral neck, which is predominately cortical bone, increased the graft material by 15% and does not affect the compressive stiffness.

2.5 Graft substitutes

Although allogenic bone is more readily available than autograft, its supply is still very limited and often falls short of demand (Galea at al, 1998). Consequently the requirement for, and research into alternatives is high. Xenografts (from another species) have been used in the past, however they require a lot of processing to reduce the immunogenicity to an acceptable level, they suffer from ethical controversy and there are fears of virus or prion transfer (Moreau et al, 2000). Other natural materials such as coral and ivory have also been investigated (Moreau et al, 2000), but synthetic grafts of natural origin are favoured. Hydroxyapatite (HA) [Ca_{10} $(PO_4)_6$ $(OH)_2$] is a naturally occurring mineral, which is the very similar to the principle component of the inorganic mineral phase of bone. The inorganic phase accounts for 60 to 70 % of bone tissue (Bostrom et al, 1999).

HA is one of many Calcium Phosphate ceramics. Another commonly researched is Tricalcium Phosphate (TCP) [$Ca_3(PO_4)_2$]. Both TCP and HA have been used on their own and in combination in orthopaedic applications, particularly for the coating of uncemented implants. The preparation of Calcium Phosphates usually involves compaction of powder to create a structure commonly known as a "green" state; this is then sintered at temperatures from 1100°C to 1300°C. Sintering of the material fuses the individual crystals at the crystal grain boundaries. The fabrication process has developed to enable pores to be created in the sintered structure. One such method is including naphthalene particles in the original compaction, these are then removed by sublimation before sintering of the green state material (Jarcho, 1981). The coating of prostheses is performed by plasma spraying; a stream of mixed gases passes through a high energy electric arc struck between two electrodes, the powder is suspended in the gas stream and fed into the plasma flame causing it to hit the prosthesis surface with high energy forming a physiochemical bond (Geesink; 1990).

Calcium Phosphate granules could be used on their own or as a mixture with bone chips for impaction grafting. This would help alleviate problems of obtaining allograft and individual use would eliminate concerns of infections from donor bone. They should also offer osteoconductive properties. Most Calcium Phosphates, except HA have the ability to resorb in physiological conditions, HA is the only thermodynamically stable Calcium Phosphate above pH 4.2, (the normal physiological pH is 7.2) and it is debatable as to what extent it will resorb (Calcium Phosphate biomaterials, 2003). Consequently it is common for TCP to mixed with HA creating a biphasic ceramic that will resorb to some extent, but not at the speed of TCP alone (Geesink; 1990). The resorption rate of Calcium Phosphates is also affected by the micro and macroporosity of the structure and the interconnectivity and organisation of the pores, although the ideal structure for bone ingrowth is still under debate. In addition to the biological properties of these ceramics, the initial mechanical properties and those during incorporation with bone are important. In general they are said to have similar stiffness to cancellous bone, however as the structure is altered to enhance the biological union, the mechanical properties will also change.

A common in-vivo method of testing ceramics is insertion of granules or a cylindrical block into the distal femur or proximal tibia of rabbits (Eggli et al, 1999; Gauthier et al, 1998; Chang et al, 2000; Yano et al, 2000; Orr et al, 2001). Assessment of the results must take into consideration that this is not the same as around a revision prosthesis as there is no direct loading to the graft. Another limitation is that the bone defect was created immediately before grafting and was surrounded by bone with an abundant blood supply.

The porosity of ceramics plays a role in remodelling, as the size of the pores should allow for vascular and bone ingrowth. Findings of in-vivo studies may also be relevant to the packing of allograft chips because dense packing and size grading will reduce porosity. Eggli et al (1999) found better infiltration of bone into HA and TCP 60% porous cylinders with a pore size of 50 – 100 μm compared to 200 – 400 μm. However in the cylinders with small pores interconnecting channels of ~ 20 μm were frequently found, but in the large pore cylinders these interconnecting channels were only rarely found. The interconnecting pores were too small to accommodate cells however they may, in some unkown way, have attributed to the superiority of the small pore blocks. The study also demonstrated the greater resorption of TCP compared with the HA. In a study of a biphasic composite of 60 % HA and 40% TCP, cylinders with a pore size of 565 μm had more newly formed bone than those with 300 μm pores (Gauthier et al, 1998). They also investigated the effect of percentage porosity but found no significant difference in bone ingrowth between 40 and 50 % porosity, perhaps because the difference in the porosity level between the too were too low. Chang et al (2000) found an optimal pore size of 300 μm, compared with 50 μm, 100 μm and 500 μm. They were also able to show increase in ultimate compressive strength eight weeks after implantation.

Yano et al (2000) investigated the mechanical properties of incorporating HA granules but they compared this with allograft particles. The results of the allograft samples showed that at three weeks the mixture of woven bone and bone chips did not show a yield point under mechanical loading and were considered to be structurally immature. However, by eight weeks the graft did exhibit a yield point and had stiffness similar to normal cancellous bone. The HA granules had a higher initial strength and stiffness than rabbit cancellouse bone at three weeks. By eight weeks the mechanical properties had reduced and were similar to cancellous bone, but these increased again by 12 weeks. It was discussed that resorption of the new bone, due to lack of weight bearing, caused the loss in stiffness. Thickening and maturing of the trabeculae between eight and 12 weeks reversed this affect. The HA granules exhibited their osteoinductive properties by extensive bone apposition at three weeks, however the granules did not become resorbed by 12 weeks. Orr et al (2001) also studied the mechanical properties of remodelling HA and reported that at 26 weeks post implantation the graft had an elastic modulus nine times that of the surrounding cancellous bone. This could be due to large amounts of new bone formation contributing to the composite modulus of the bonded HA and bone.

Pratt et al (2002) used an ovine defect model to assess morsellised bone graft expanded by 50 % with HA / TCP granules. Two HA / TCP ratios of 80/20 and 20/80 were used. They graded the particles following the soil mechanics theory described by Brewster et al (1999). In addition they used a simplified version of two thirds small particles and one third large particles (by weight) to produce a clinical control of allograft and another version of 50 % allograft and 50 % HA / TCP 80/20. The results found improved performance with graft consisting of higher TCP than HA, and also with graft created by grading of three particle sizes (rather than eight) in the groups containing 80/20 HA / TCP. The initial porosity of the HA/TCP granules is not discussed, but it is possible that reducing the grading created a less dense structure that was more osteoconductive. Stryker Howmedica currently market the 80% TCP / 20% HA granules as BoneSave™ in sizes of 2 – 4 mm and 4 - 6mm.

Blom et al, (2001) also conducted an ovine study of the two ratios of Calcium Phosphates, 80/20 TCP/HA (BoneSave™) and 20/80 TCP/HA as 50/50 mixes with allograft. The 20/80 TCP/HA was also studied with just 10 % allograft and 90 % substitute, 100 % allograft was used as a control. This hemi arthroplasty model allowed for functional loading of the graft in a method more comparable with human femoral impaction grafting, and was left in situ for 18 months. There appeared to be a trend indicating more osteogenic response in the 10 % allograft group, but this was not significant. Blom et al (2002) also performed a time zero stability study of BoneSave™ as 50/50 and 90/10 mixes with bone graft, with a control of 100 % bone graft. The bone graft was prepared from sheep humeral heads, and milled in a Norfolk bone mill (Stryker). Although the experimental set-up was simple (the graft was impacted into a tube, a sheep size prosthesis was cemented in place, and direct axial loading of the femoral head was conducted) a significant reduction in subsidence was observed in the groups containing BoneSave™. After the final loading phase of 800 N the subsidence was significantly less in the 90 % BoneSave™ than the 50 % BoneSave™ group.

Bolder et al (2002) performed a number of experiments in an acetabular defect model comparing morsellised bone graft with different sizes of HA/TCP granules, on their own or mixed with bone graft. Although they found reduced migration in the groups containing TCP/HA granules (with the 6 – 8 mm performing better than the 3 – 5 mm particles) they expressed concern that this was a result of cement penetration, which clinically would prevent revascularisation. Therefore they recommended small particles of such substitutes and mix with bone graft to limit the cement penetration. Following a simple conical femoral impaction grafting model Grimm et al (2001) also advise against the use of Calcium Phosphate granules on their own. They are concerned by their lack of visco-elastic properties and believe that on their own they might produce potentially damaging wear particles. Their study found improved results with 2 – 4 mm particles compared with 1 – 2 mm and 4 - 6.3 mm. The largest size group probably produced poor results because the cylinder they were impacted into was only a 20 mm diameter, leaving little space once the conical impactor had been driven in. Even with current impaction of allograft, larger chips are more commonly used in the acetabulum than in the femur.

The compressive strength of HA has also been investigated with regard to porosity and pore sizes ranging from 5 – 400 μm (Huec et al, 1995). As one would expect, an increase in porosity correlated with decreased strength, however the blocks with smaller pore sizes had higher stiffness than those with larger pores sizes.

Calcium phosphate granules have been used successfully in revision hip arthroplasty surgery (Schwartz et al, 1999; Oonishi, 1991). Oonishi (1991) has used HA in the acetabuli of thirty patients and suggests it is more stable than allograft as a fibrous tissue interface is unlikely to develop between the cement and HA granules, which might be experienced between the cement and bone. Schwartz et al (1999) used two types of substitutes in acetabuli and femoral hip revisions, the first was 55% HA / 45% TCP with 60% interconnective porosity of 400 μm pores. The second graft type was 65% HA and 35% TCP and only had 40 % porosity, the pores were 150-200 μm and situated mainly on the surface and with only partial interconnectivity. The first graft type was available in 2 – 3 mm granules form and the second as cubes, sticks, disks and wedges. The authors used these two graft types without the addition of allograft in 29 acetabular revisions and 43 femoral revisions. Radiological incorporation of the grafts was seen and some histology showed resorption of the ceramics and bone reconstruction.

Johnson at al (1996) looked at the affect of adding bone marrow aspirate to biphasic HA and TCP in a canine radius model. The results found improved biomechanical and radiographic results. It is possible that the future of synthetic bone grafts may lie in such biological additives.

Calcium phosphates are a form of biomaterial. Another type of biomaterial that has been researched for orthopaedics is silica based glasses or glass ceramics. These bioglasses have been shown to have excellent biocompatibility and promote bone growth during their resorption process (Meseguer-Olmo et al, 2002). In addition these bioglasses have been used to reinforce HA, resulting in a higher bonding force that HA alone in a push out test at 16 weeks in rabbits (Lopes et al, 2001). However bioglasses are not poular for bone grafts as they are a very brittle.

Another Calcium Phosphate bone graft that has been developed for impaction grafting applications is ApaPore-60[1], this is a totally pure HA with no secondary phases. The

[1] ApaTech Limited, Queen Mary, University of London, Mile End Road, London, E1 4NS

material is stochiometric having a Calcium to Phosphorous ratio of 1.67. This pure HA has been shown to maximise favourable bony response (Hing et al, 1998). ApaPore-60 is 60 % porous and consists of a macroporous structure with microporous interconnectivity. The macro porosity is said to facilitate angiogenesis, avoid mechanical discontinuity and maintain long term osseous integration, while the interconnective microporosity allows nutrient transfer to host bone, stimulates cell differentiation, promotes revascularisation, allows fast bone ingrowth, enhances long term stability and provides a continuous host bone/graft composite (ApaPore Stimulating stable integrated bone repair; Hing et al, 2002).

With so many different studies on the properties of Calcium Phosphates with regard to their chemical composition, their percentage porosity, micro and macro pore sizes and interconnectivity of the pores, it is difficult to draw a conclusion as to which is the most superior biologically and mechanically.

Chapter 3

Modification of Exeter Slap Hammer for Force Measurements

3.1 Introduction

Since its development in the early 90's femoral impaction grafting has been the subject of debate. The creators of the technique have written encouraging papers on its outcome, whilst others have had less favourable results. In particular problems associated with rotation and subsidence of the stem are common (see main introductory chapter and literature review of this thesis). Unfortunately there are a huge number of variables related with this technique, the following being just a few: initial condition of the femur, type of graft used, surgical technique, postoperative weight bearing and stem design. Research on the allograft used has followed, often in relation to impaction. However the surgeon's technique is as yet unquantified. In order to understand and develop the femoral impaction grafting procedure it is necessary to first evaluate the current technique. It was decided that the slap hammer used with the Exeter X-change Revision System would be modified to enable intra-operative force measurements to be taken so that a thorough investigation into the technique and the variability between surgeons could be carried out. In addition these measurements would be of used for future experiments so that the mechanical and biological properties of impacted allograft and bone substitute materials could be studied under realistic conditions.

The Exeter X-change revision system was the first of its kind and is the most commonly used in the United Kingdom for impaction grafting. It was therefore decided that the measurements should be based on this system. The Exeter X-change revision instruments were developed specially for impaction grafting. On the femoral side there is a slap hammer that can be used to impact the graft using distal or proximal impactors. The Exeter X-change kit is illustrated in Figure 3.1 and includes a slap hammer, distal and proximal impactors.

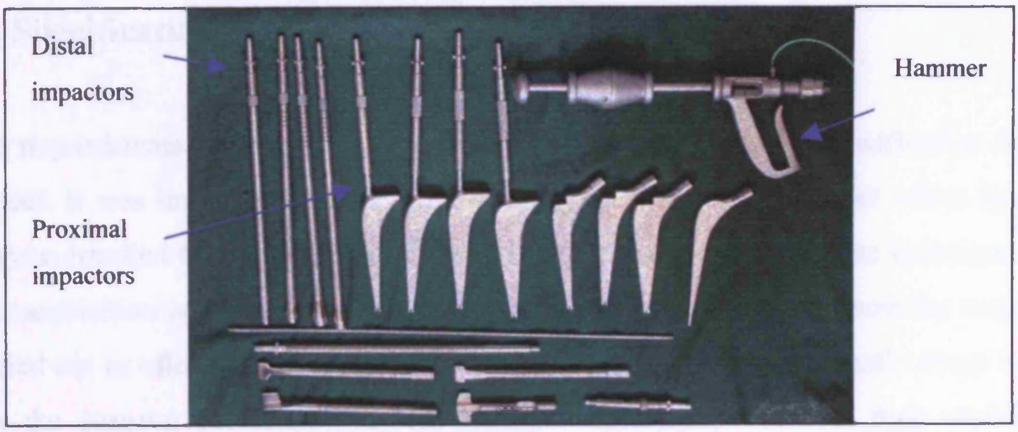

Figure 3.1 - Exeter X-change femoral revision instruments.

Aim

To create a method of measuring the forces applied by the surgeon during surgery to impact the morsellised graft down the femur, using the Exeter X-change slap hammer.

This idea to instrument the hammer originated as part of a final year MEng project in mechanical engineering at Bath University (Phipps, 2000). It was during this project that the specifications and initial modification ideas for the hammer were developed. The final design, production and calibration were carried out during this PhD project.

3.2 Specification

The requirements of the modification were evaluated to create a specification for the project. It was important that any modification of the hammer did not effect how the surgeon handled the hammer as this may have inadvertently effect the technique. The data acquisition would have to be performed so that it does not effect how the surgery is carried out or effect the surgical time by more than a few minutes. Ideally every impact that the surgeon performs with the hammer should be recorded, thus enabling a complete picture of the quantity of energy used during the surgery as well as the magnitude of the forces. Correlation between the measurements and the type of impaction being performed (distal or proximal) is important to gain a full understanding of the technique.

Surgical instruments are normally sterilized in a superheated steam autoclave, where temperatures reach 140°C. Hospitals sterilize the equipment the day or night before any given surgery. Ideally the measuring device had to withstand autoclaving, although etholine oxide sterilization of the device was an option. However this is expensive and time consuming since it has to be sent away and cannot be carried out in the hospital. Even if the modified hammer were unable to withstand autoclaving it would still have to be washed for decontaminating after surgery.

Key point specification list:

- Easy to use by the surgeon
- Must not affect the surgery
- Record of the magnitude of each impact
- Record every impact the surgeon makes
- Log of which impactor is used for each recorded force reading
- Ability to wash the hammer once modified
- Ability to sterilize the hammer once modified, preferably through steam autoclaving at 140°C

3.3 Initial Solution

The work of the MEng project (Phipps, 2000) suggested that a method of measuring force was to mount a load washer in the hammer. It was considered easier to instrument the hammer rather than all the impactors. So at the start of this PhD study a Piezo-electric load washer was mounted in the Exeter X-change hammer (Mark II). The hammer has a 4.4 mm hole running through its centre, which the guide wire passes through. The guide wire screws into the bone plug at the distal end of the femur and helps to ensure that the graft and new femoral component are impacted centrally. Load washers are designed to be fixed in place with a central thinned preloading bolt. However, after consultation with the manufacturer, a M10 stud with a 4.2 mm hole through the centre, to accommodate the guide wire, was used instead. Figure 3.2 shows the modified hammer and an unmodified hammer from the Exeter X-change impaction grafting set. The load washer, method of recording its output, and calibration are described below.

Figure 3.2 - Modified hammer containing load washer (top) with an unmodified hammer (bottom) from the Exeter X-change Impaction Grafting Kit

3.3a The load washer

Piezoelectric devices are small and accurate for their working range, hence the Kistler Type 9102A[1] load washer with a force range of 50 kN was selected to fit in the hammer (the full data sheet for the Type 9102A can be found in the Appendix 1). Piezo-electric load washers contain quartz crystal, which yields an electrical charge when compressed; this is comparable with the force applied. The charge can be converted into voltage through a charge amplifier, so the signal can be captured and recorded. Connection between the sensor and amplifier is via a thin cable. The sensor is hermetically sealed and to protect the sensor during autoclaving a three-meter industrial cable was welded to it. At the far end of the cable a specially designed sealing cap[1] for autoclaving was made, giving a protection rating of IP 65[2]. To use the modified hammer during an operation the surgeon would have to pass the end of the cable to the operator outside the sterile area, consequently this end would no longer be sterile. The operator would then removes the sealing cap and connect the cable to the charge amplifier. At the end of an operation the sealing cap would be reconnected to the cable end so that the hammer could be decontaminated.

3.3b Charge Amplifier

To convert the Load washer signal from charge to a proportional voltage a charge amplifier was required. Kistler currently market a 50 kHz and a 200 kHz charge amplifier. Initially a charge amplifier that operated at 180 kHz was borrowed, frequency analysis of an impact waveform was conducted, which found that the high frequency charge amplifier of 200 kHz, Kistler Type 5011B[1], was required. The sensitivity value of the piezo-electric device being used should be set into the charge amplifier in pC/N. This value was ascertained in the static calibration described below (Section **3.3d**). The scale factor required in N/v should also be set in the charge amplifier. For this application it was necessary to use a scale factor such that the output stayed within the ± 10 volts range of the data acquisition card described below. The amplifier has three time constant measurements; long, medium and short. The long time constant is used for static calibration whilst medium and short can be used for dynamic measurements.

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[1] Kistler Instruments Ltd. Alresford House, Mill Lane, Alton, Hampshire, GU34 2QJ54

[2] IP 65 – Protection rating against dust and water

There is also a low pass filter on the charge amplifier, which was not required for these measurements.

3.3c Data Acquisition

Oscilloscopes and voltmeters can be used to observe the voltage output from charge amplifier, although this is acceptable for monitoring static loading, eg calibration. When loaded dynamically the speed of the waveform is too fast for the observer to monitor accurately. Storage oscilloscopes can be used to store short periods of dynamic data for immediate analysis, however given the nature of this project it was decided that the signal from the charge amplifier should be sent directly to a laptop computer for storage and analysis. For this reason it was necessary to use an analogue to digital data acquisition card, so that it was possible to monitor and store the signal on the laptop computer. Initially a program called Das Wizard[1] was selected to monitor the signal in conjunction with PC – Card Das16 /16[1]. The card was able to convert data at 200 kHz and could support 15 single ended or 7 differential analogue inputs, but when processing more than one channel its speed was reduced. Only one channel was required for this arrangement and it was set up with a differential input as this is more accurate and reduces noise. Since the charge amplifier was operating at 200 kHz, and the impulse being measured was known to be of high speed with high frequency resonance in it, it was deemed important to continue logging at 200 kHz.

The Das wizard program is an add-in it to Microsoft Excel, so all data could be recorded in data logging units, or volts straight into Excel. This was extremely useful during the early work with calibrating the load washer. However during an operation the surgeon may hit the hammer several hundred times, although these can split into several smaller batches of impacts. The surgeon will break off from hammering to add more graft or to change the impactor. Each batch of hitting may last from a few seconds to one minute; one minute of data recorded at 200 kHz is 12,000,000 points of data. Once a period of data has been recorded, each waveform then has to be extracted from these figures. Each waveform lasts only a few milliseconds. The quantity of data to be recorded and then analysed was more than Excel could handle so a more advanced program was

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[1] Computer Boards, 16 Commerce Boulevard, Middleboro, MA 02346, USA

required. A special Labview[1] program was written by Alan Watkins (SkyLark Technology) for this application to record and analyse the data during surgery. Labview is a type of Software designed for testing, measuring and control.

The Labview program was able to log the data at 200 kHz and record short sets of data at a time with less than a second gap before recording again. After observing the surgical technique, it was decided that recording data in batches of 20 seconds would be ideal. The Labview program had a front view panel, illustrated in Figure 3.3, where the following could be input: recording frequency, number of samples to be recorded in a batch and calibration factor matching the charge amplifier. From the front panel the operator could chose to either log data, display the data or analyse the data. The data logging panel is shown in Figure 3.4. To commence data logging the "Start data logging" button was selected; the button then turned green to indicate that the data was being recorded. Once a file has been saved the button returned to yellow, and the file name for the recorded data appeared in the "first file name" box, the file name was related to date and time of capture. Once a file had been recorded the "Start data logging" button could be selected again to record another series of data, with approximately only half a seconds gap between files, or the "return to main menu" button could be selected to return to the main menu. Display data (Figure 3.5) could be used to view the recorded data in frames of five seconds, giving a quick overview of the results. The individual waveforms were analysed in the processing data panel, (Figure 3.6). A search threshold was inserted and each waveform containing a value above the given threshold was found. The data surrounding this point was then displayed. Every impact in a file could be examined in detail in this manner. A peak value was obtained for each waveform; this value was measured in relation to the signal prior to the start of the impact waveform. The reading at the beginning of an impact was not necessarily zero, as the surgeon could have been applying a pressure. Once the program had finished analyzing a file, the data points of each impact were stored in one text file and a list of the peak forces were stored in another text file.

[1] National Instruments, Measurement House, London Road, Newbury, Berkshire RG14 2PS

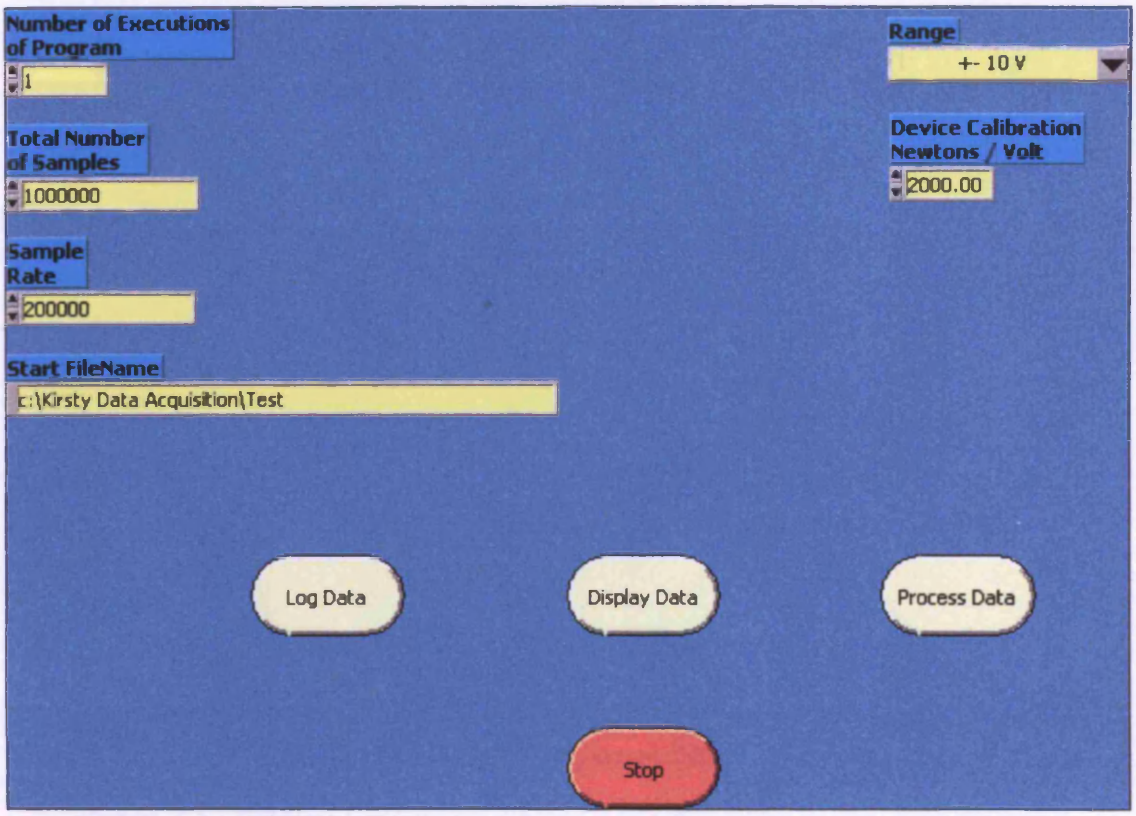

Figure 3.3 - Labview Front Panel

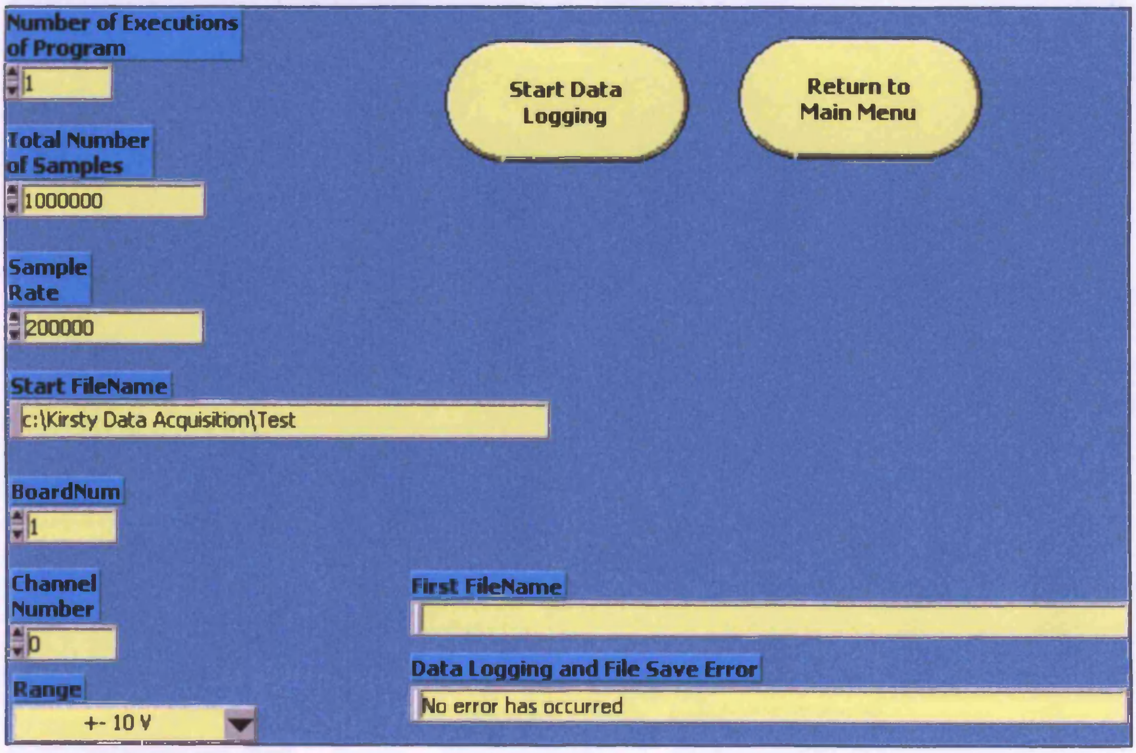

Figure 3.4 - Data Logging Panel

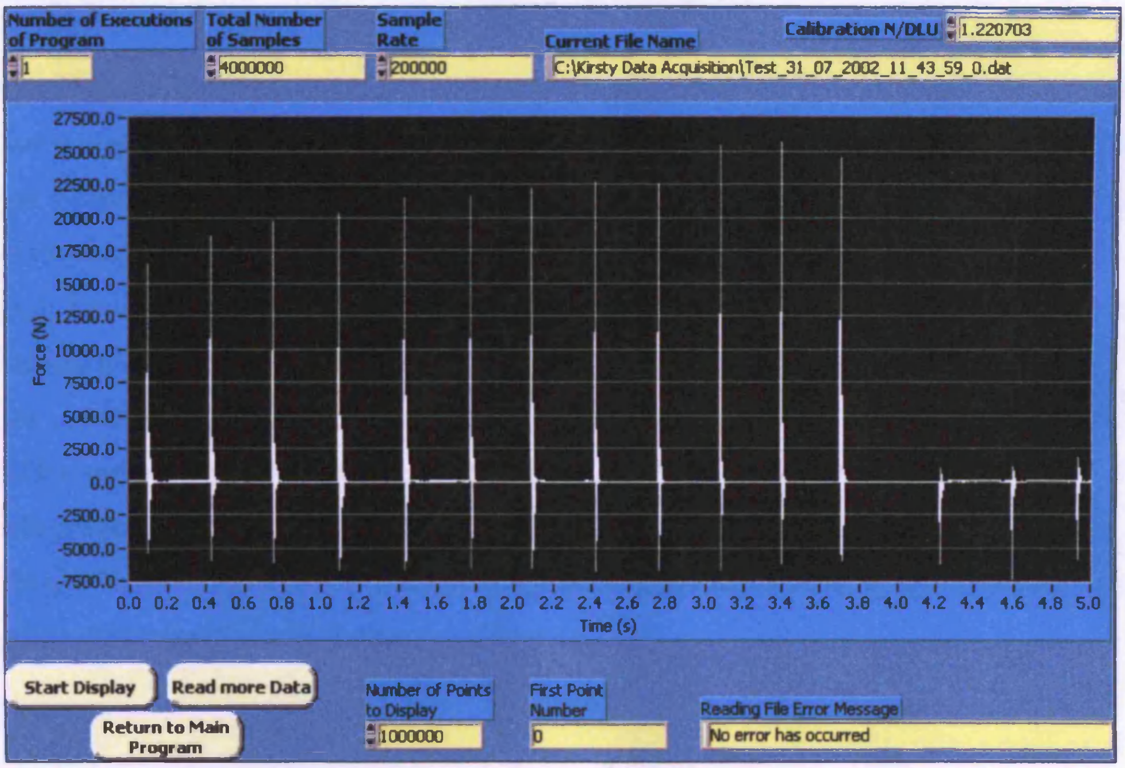

Figure 3.5 - Display Data panel, Shows 5 second frames of the recorded data

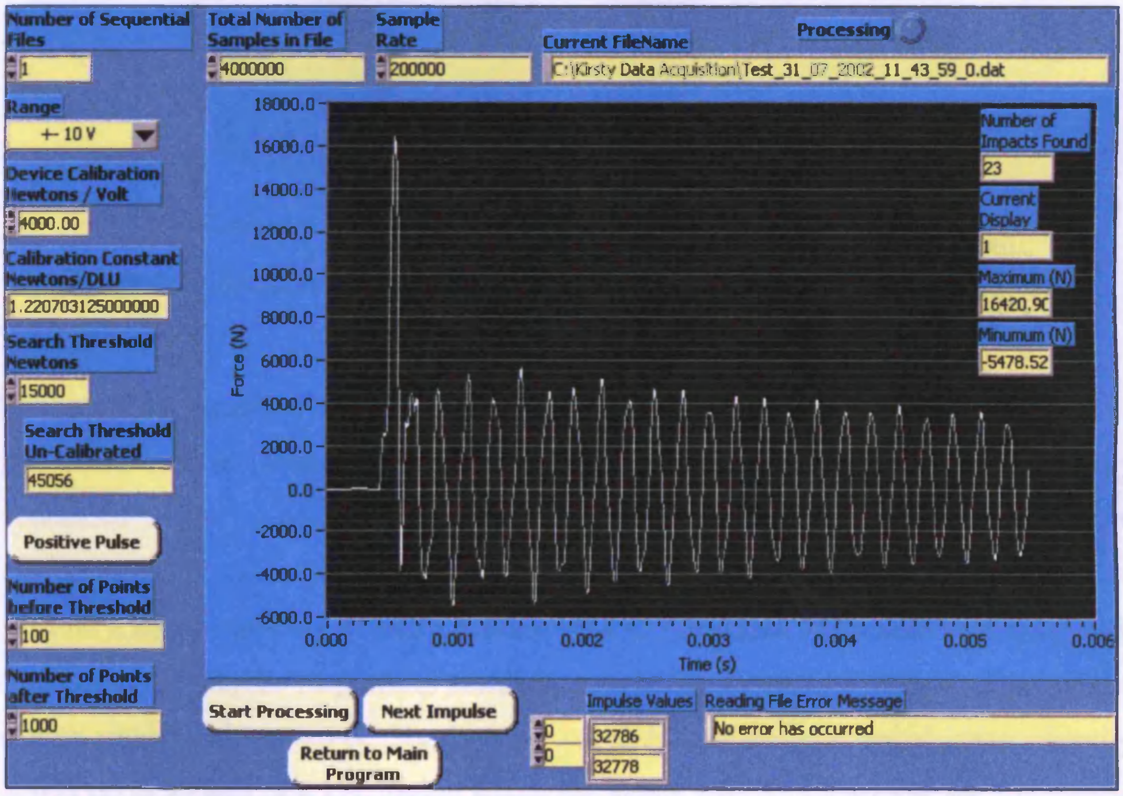

Figure 3.6 - Processing Data panel, processes and displays each force profile

3.3d Static Calibration of the Load Washer

The load washer is an industrial type and was not pre-calibrated. However the washer had a stated approximate un-mounted sensitivity value of - 4.3 pC/N (pico Coulumbs per Newton). It is designed to be mounted with a bolt through its centre, which ensures even contact with the surfaces and by tightening the bolt a preload is applied so that both tensile and compressive forces can be measured. However the preloading bolt creates a force shunt, where part of the force to be measured flows via the bolt and is not measured by the sensor. Consequently calibration to determine the sensitivity value of the sensor is required once preloaded in situ. Kistler recommends the use of a thinned M8 preloading bolt to minimise the force shunt, as illustrated in Figure 3.7. However, for the hammer mounting a hollow M10 bolt was chosen instead to accommodate the guide wire passing down the centre of the hammer.

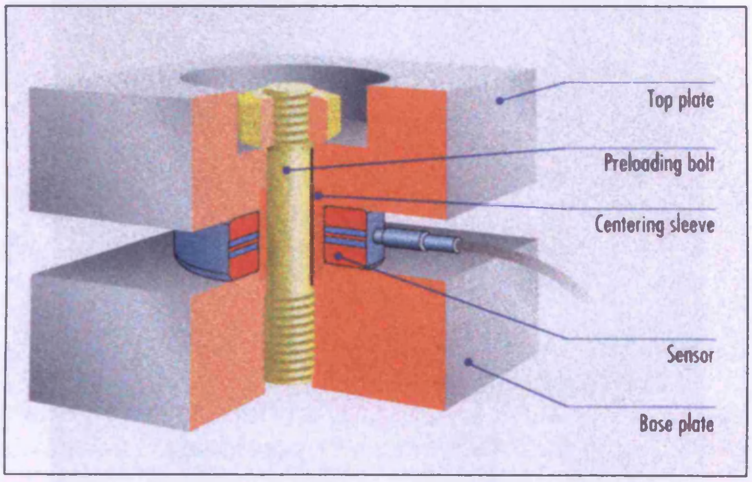

Figure 3.7 - Recommended mounting of a Load Washer using a preloading bolt

To obtain an accurate sensitivity value for the load washer, static calibration was performed once the sensor had been preloaded into the hammer. Static calibration was conducted in the Hounsfield Loading machine[1], see Figure 3.8. For calibration the charge amplifier time constant has to be set to long. In this configuration the signal is held for a significant period before drifting back towards zero and a voltmeter was used to observe the output. To perform calibration an initial sensitivity value was set on the charge amplifier (p = - 4.3 pC/N), the load was then increased in steps of approximately 250 N up to a value of 4 kN, during which the output voltage values and applied forces were recorded. The results were then manipulated to find the desired sensitivity level,

[1] Hounsfield (H series 10M). 6 Perrywood Business Park, Salfords, Surrey RH1 5DZ

and the test was repeated to check the selected pC/N value. Unfortunately the calibration curve of the sensor does have some variation in linearity and hysteresis (Appendix 1, Figure 1A), so ideally the static calibration should coincide with the force range used dynamically. However the hammer can tolerate higher forces dynamically than was safe to test statically, hence calibration was only conducted up to 4 kN. Any loosening of the preloading bolt could change the sensitivity, consequently it was decided that calibration should to be performed after every surgery.

Figure 3.8 - Static calibration, performed in the Hounsfield, of load washer mounted in the slap hammer

3.4 Development of Force measurement

Once the load washer had been mounted in the hammer and static calibration performed, dynamic measurements could be taken. To test the dynamic measurements the hammer was clamped over a solid surface and the mass dropped down the full height of the hammer. The waveforms produced, Figure 3.9 A, did not have a clear initial peak, which had been expected from trials with the simplified hammer. This made it difficult to have confidence that the peak value did correspond to the applied force. In surgery the hammer would be impacting bone chips, which are relatively soft in relation to the metal, so readings were repeated over bone chips. A surgeon impacted fatty bone chips into a plastic, femoral Sawbone[1] mimicking the surgical procedure; Figure 3.9 B is an example of one of the impacts. The waveforms were all very similar for each set of impactions. As the graft became more impacted and stiffer the amplitude of each waveform increasing slightly. Unfortunately there was still no clear initial peak representing the applied force. To evaluate the waveforms further Fourier analysis was performed on the data to establish the dominant frequencies. Figure 3.10 A and B shows the frequency spectrum from zero to 30 kHz, there were negligible frequency spikes after this frequency. In general there were two dominant frequencies from hitting the bone chips; 2 kHz and 19 kHz. However when hitting the metal there appeared to be a dominant frequency below 1 kHz and one around 12 kHz. Contrary to the prediction, the force profile from hitting bone chips did not have less resonance than hitting metal.

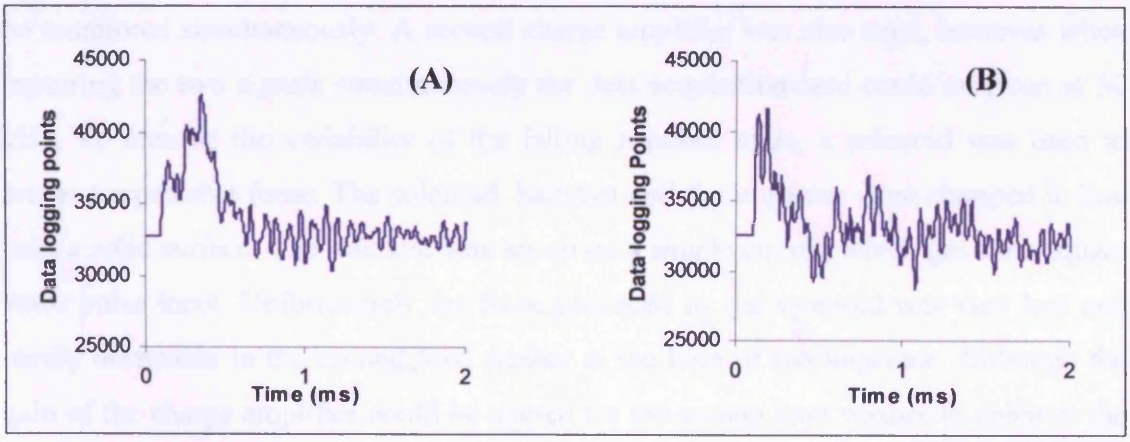

Figure 3.9 - Waveforms produced by hitting (A) a hard surface and (B) hitting fatty bone chips

[1] Pacific Research **Sawbones Europe AB,** Krossverksgatan 3, 216 16 Malmö, Sweden

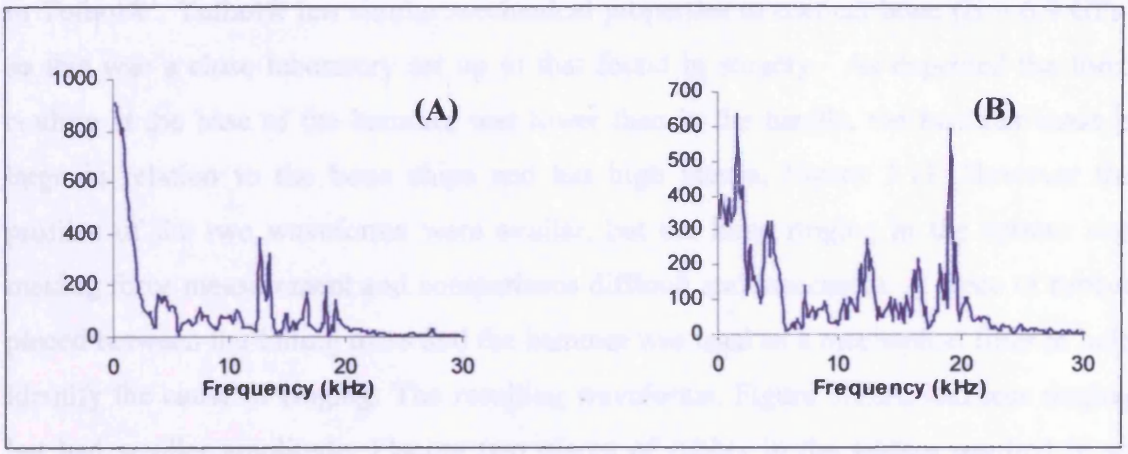

Figure 3.10 - Fourier analysis of waveform produced from hammer mass when: (A) clamped over a hard surface and (B) hitting fatty bone chips

It was therefore decided that the dynamics of the structure had been under estimated, and that the force readings in the middle of the hammer were not measuring the applied force of the surgeon or the force applied to the bone chips at the distal end of the hammer and impactors. To discover if there was a relationship between the force readings in the middle of the hammer and the force imparted by the hammer to the bone chips, the load washer was mounted at the end of the distal impactor. The resulting waveforms looked similar, but their values were smaller. To establish a relationship between the readings in the hammer and in the impactor, a second load washer was used so that the force profile in the middle of the hammer and the end of the impactor could be monitored simultaneously. A second charge amplifier was also used, however when capturing the two signals simultaneously the data acquisition card could only run at 50 kHz. To remove the variability of the falling hammer mass, a solenoid was used to create a repeatable force. The solenoid, hammer and the impactor were clamped in line onto a solid surface. The solenoid was set up on a simple circuit, which gave the square wave pulse input. Unfortunately the force produced by the solenoid was very low and hardly detectable in the second load washer at the base of the impactor. Although the gain of the charge amplifier could be altered for the second load washer to enhance the signal, the noise was large in relation to the signal. Although the solenoid had not been able to give the desired results, it was now possible to measure from both load washers simultaneously.

A comparison of the two load washer readings was performed over bone chips mounted in Tufnol®[1]. Tufnol® has similar mechanical properties to cortical bone (E = 6.9 GPa) so this was a close laboratory set up to that found in surgery. As expected the force reading at the base of the hammer was lower than in the handle, the hammer mass is large in relation to the bone chips and has high inertia, Figure 3.11. However the profiles of the two waveforms were similar, but the large ringing in the system was making force measurement and comparisons difficult and inaccurate. A piece of rubber placed between the falling mass and the hammer was used as a mechanical filter to help identify the cause of ringing. The resulting waveforms, Figure 3.12A, had less ringing but had smaller amplitude. Placing two pieces of rubber in the system resulted in an even greater reduction in force and ringing, Figure 3.12B. Although this drop in ringing made force measurement easier, it was by its very being reducing the force, which was not acceptable. Since a mechanical filter was considered unsuitable, the electrical filter of the charge amplifier was tried. The Kistler charge amplifier type 5011 has the option of a low pass filter at 10, 30, 100, 300 Hz and 1, 3, 10, 100 kHz. To decide what filter should be used, the natural frequency of each part of the system was estimated through simple calculations.

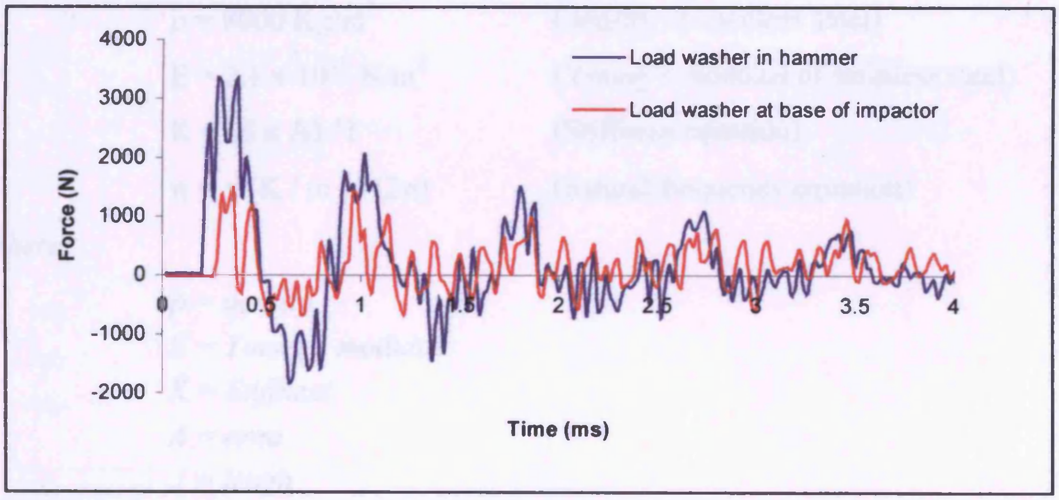

Figure 3.11 - Force profile comparison from in the hammer and impactor, when hitting bone chips into a Tufnol dish

[1] RS Green Lane, The Fairway Estate, Hounslow, Middlesex, TW6BU

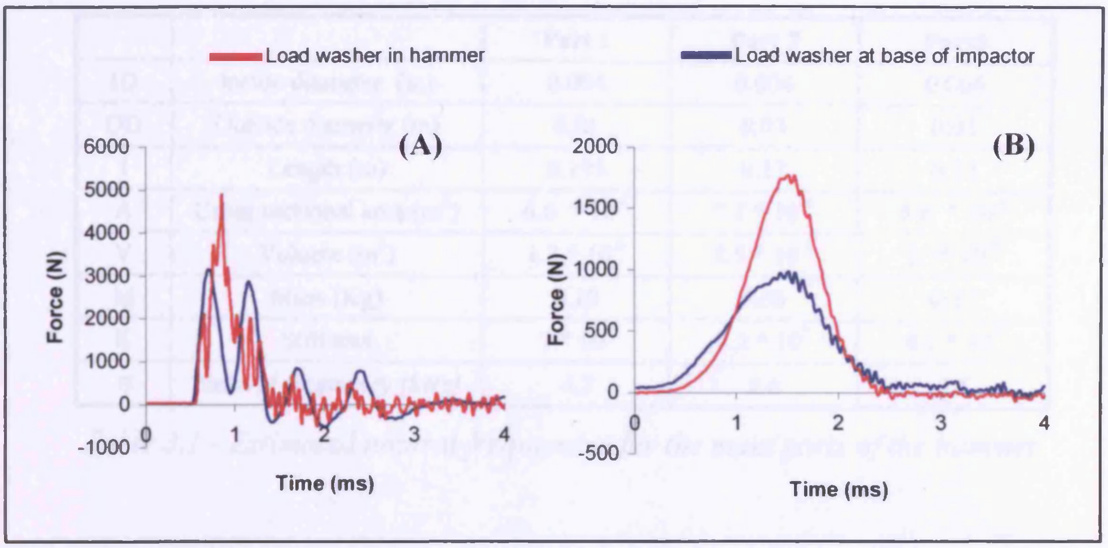

Figure 3-12 -Force profiles from hammer and impactor with (A) 1 piece of rubber and (B) 2 pieces of rubber between the hammer mass and handle

To establish what filter to use, simple calculations were performed to estimate the natural frequencies of each of the main parts of the hammer using the following values and formulae:

$\rho = 8000$ Kg/m^3	(density of stainless steel)
$E = 2.1 \times 10^{11}$ N/m^2	(Young's modulus of stainless steel)
$K = (E \times A) / l$	(Stiffness equation)
$\eta = \sqrt{(K / m)} / (2\pi)$	(natural frequency equation)

Where:

ρ = density
E = Young's modulus
K = Stiffness
A = area
l = lengh
η = natural frequency
m = mass

The hammer was split into three parts and the natural frequency for each part calculated, Table 3.1. Part I was the long thin tube over which the mass slides, Part II was the dome at the top of the hammer, and Part III was the distal impactor. The shape of the handle area was too complicated to estimate a natural frequency.

		Part 1	Part 2	Part3
ID	Inside diameter (m)	0.004	0.004	0.004
OD	Outside diameter (m)	0.01	0.03	0.01
l	Length (m)	0.195	0.12	0.32
A	Cross sectional area (m^2)	$6.6 * 10^{-5}$	$7.1 * 10^{-4}$	$6.6 * 10^{-5}$
V	Volume (m^3)	$1.3 * 10^{-5}$	$8.5 * 10^{-5}$	$2.1 * 10^{-5}$
M	Mass (Kg)	0.10	0.68	0.17
K	Stiffness	$7 * 10^7$	$1.2 * 10^7$	$4.1 * 10^7$
η	***Natural frequency (kHz)***	***4.2***	***6.6***	***2.5***

Table 3.1 - Estimated natural frequencies for the main parts of the hammer

Filtering of the signal when the hammer was used to impact bone chips was performed at 3 kHz and 10 kHz, Figure 3.13 A and B. Although some of the signal resonance was reduced at 10 kHz, there was still not a distinctive peak. With the 3 kHz filter the most resonance had been removed leaving a clear initial peak. However the readings from within the impactor were still variable, making it impossible for this to be used as a calibration reference.

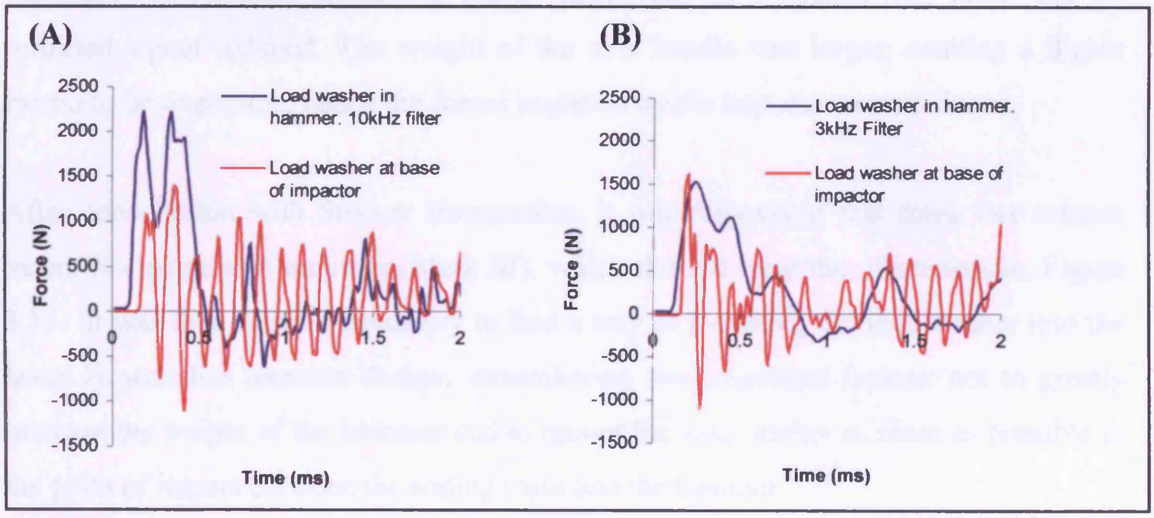

Figure 3.13 - Force readings from the hammer and base of impactor with the charge amplifier filter set to (A) 10 kHz and (B) 3 kHz

It became apparent that accurate force readings were not possible with the load washer mounted at the centre of the hammer, as the signal was extremely complex. The resonance created when the weight struck the hammer, metal hitting metal, was probably being made worse by the large handle, which was offset from the central axis of the hammer. Also stress waves appeared to be reflected back up the hammer and with the impactor attached, it appeared likely that some were being reflected at the junction between the hammer and impactor and some at the base of the impactor. It was decided that the signal would be more interpretable if the load washer were mounted closer to the point of impact of the striking mass and if there was no offset handle. To test this theory a round hammer handle was designed to replace the offset handle, which is illustrated in Figure 3.14.

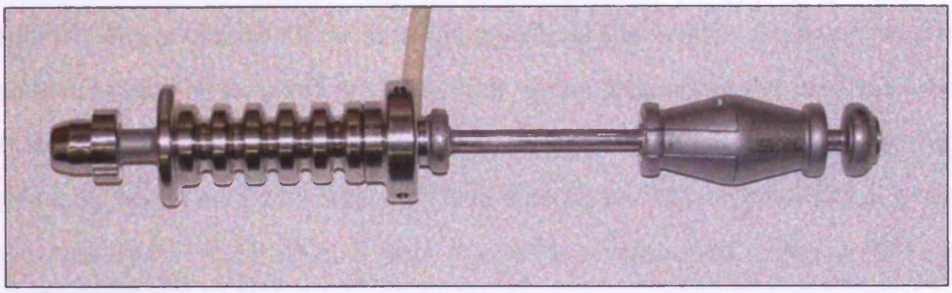

Figure 3.14 - Hammer with modified round handle

Once the hammer had been modified with the new round handle and the load washer mounted closer to the point of impact, it was possible to have confidence in the readings. The resulting signal was greatly improved; the resonance was lower and the reflected signal reduced. The weight of the new handle was larger; creating a higher inertia to be overcome, hence the forces imparted by the impactor were reduced.

After consultation with Stryker Howmedica, it was discovered that there was a more recent X-change slap hammer (Mark III), which did not have the offset handle, Figure 3.15. It was then deemed necessary to find a way of mounting the load washer into the latest Howmedica hammer design, remembering two important factors: not to greatly increase the weight of the hammer and to mount the load washer as close as possible to the point of impact between the sliding mass and the hammer.

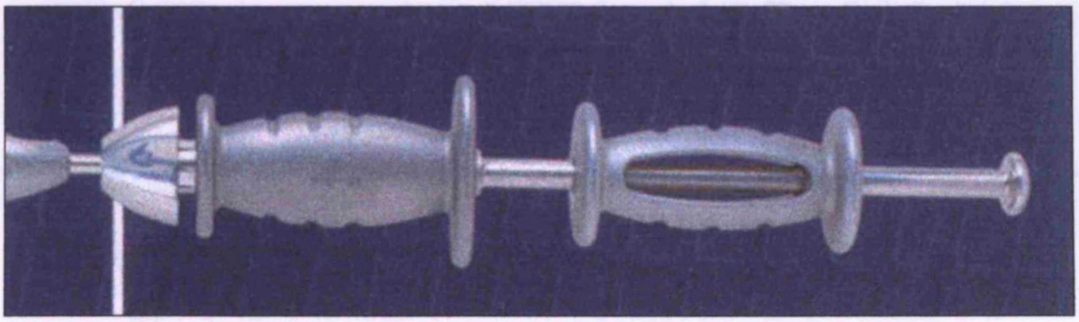

Figure 3.15 - Mark 2 Exeter X-change slap hammer

3.5 Final Solution

The final solution was to preload the Kistler Load washer (9102A) into the Mark III Exeter slap hammer at the point of contact of the sliding mass. Figure 3.16 shows the modification, the load washer is mounted only a few millimetres away from where the sliding mass hits the hammer. The Exeter Mark III hammer is fabricated for single assembly only; as each part is introduced it is welded into position. In order to modify the hammer it was necessary to cut it in the middle of the handle. An insert was made so the two halves could be screwed back together whilst preloading the load washer in situ. Another insert was made to restore the material lost during cutting and machining, the hammer handle with this insert was grit blasted to restore the original finish of the item. Prior to assembly of the completed item it was decontaminated in decon 90 in an ultra sonic water bath to remove any residue from the machining process.

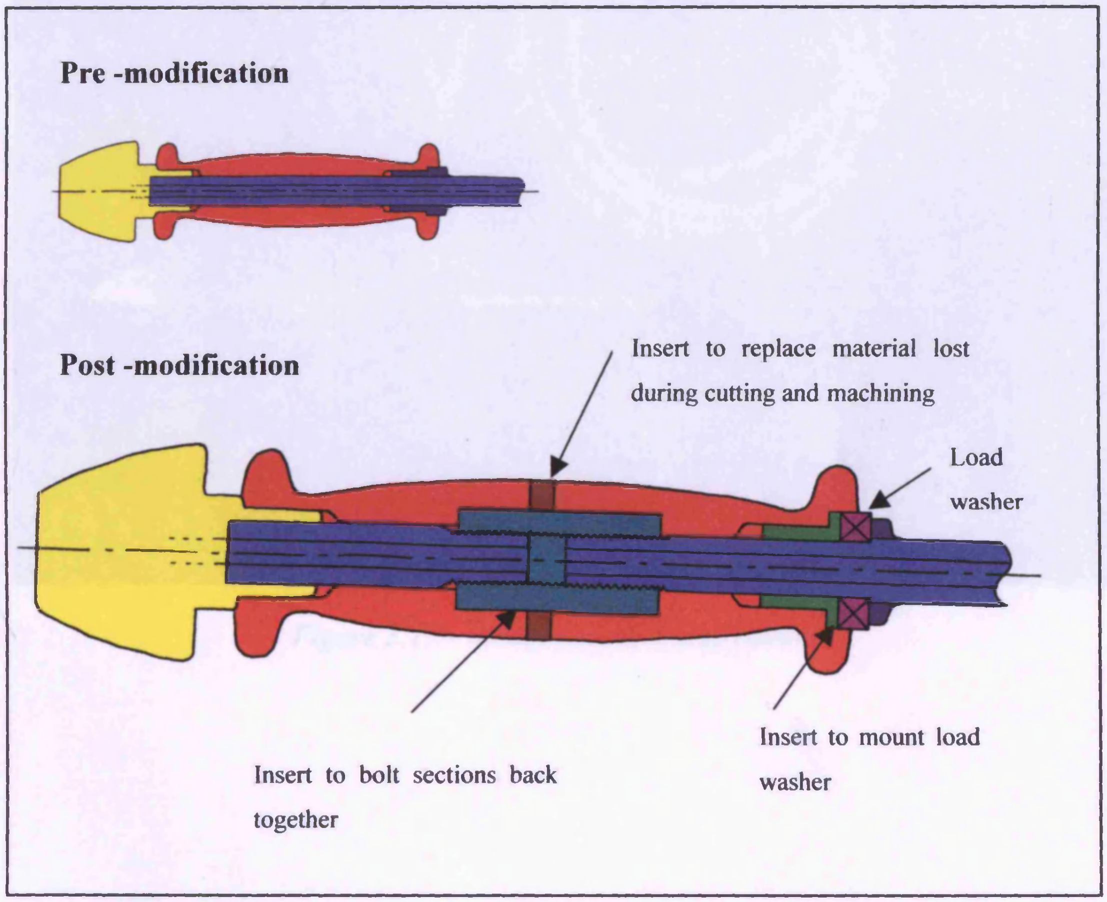

Figure 3.16 - Modification of hammer handle to mount load washer

The modified hammer with load washer is shown in Figure 3.17. A three meter long industrial cable was welded to the sensor and a special cap sealed the far end. Medical grade silicon tubing[1] with a 10 mm external diameter covered the cable to protect it during surgery. This was fixed to the hammer end using medical grade room temperature curing silicon rubber[2], and left open at the far end. Once the hammer had been assembled the calibration factor of load washer in-situ was determined by static calibration in the Hounsfield loading machine as 3.00 pC/N.

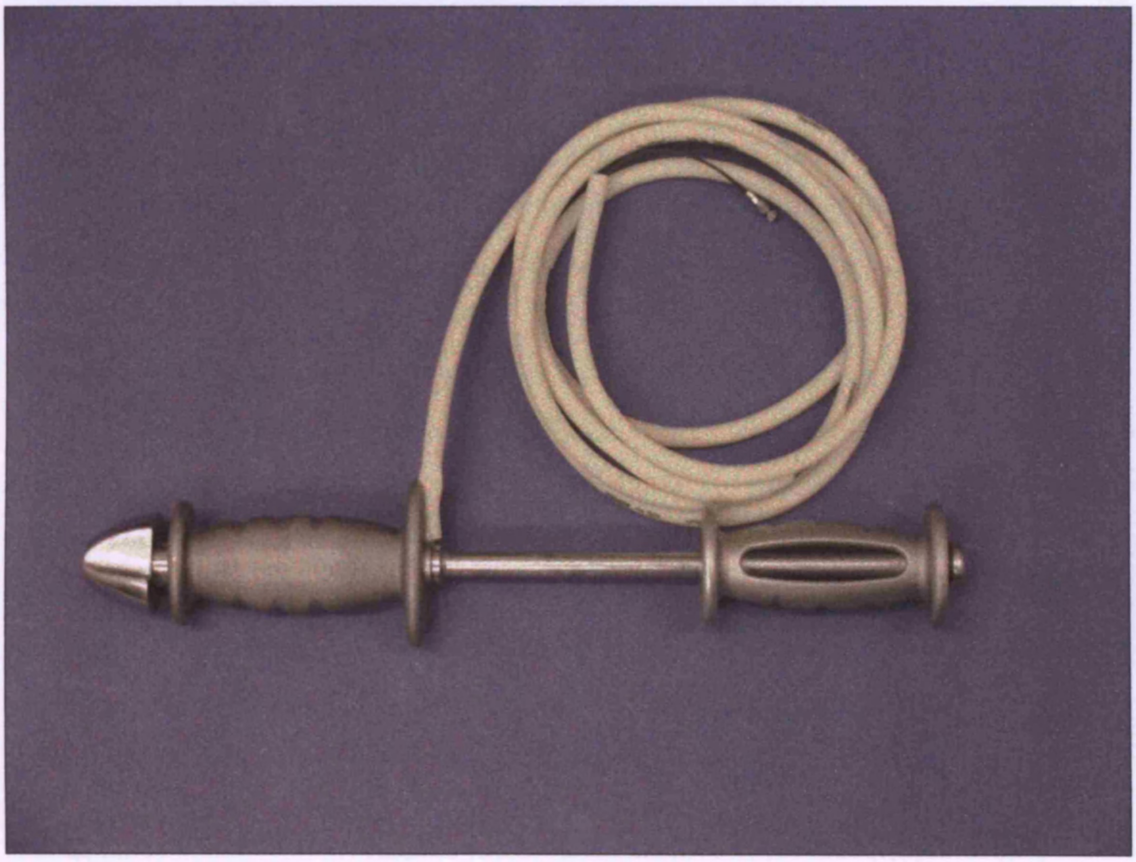

Figure 3.17 - Modified Exeter slap hammer

[1] PharMed® 3075 N.W. 107th AVENUE (Pharmed Way) Miami, Florida, USA

[2] 3140 RTV coating – Dow Corning corperation, Midland, MI, USA.

3.6 Calibration of force in the impactors

The early work on adapting the hammer had highlighted that the force measured in the hammer is not actually equivalent to the force in the impactors. The forces in the impactor are lower because the inertia involved in driving the hammer following an impact actually absorbs some of the energy. The extent to which the force is absorbed, is dependent on the material the hammer is hitting. When hitting a very hard surface, the majority of the force will be transmitted, but with a softer surface much of the force will be absorbed by the inertia of the hammer. The force readings obtained will be useful as a direct comparison between different surgeon's techniques. However to utilise the readings in other research projects, a relationship between the readings in the hammer and the force in the impactors had to be measured. To do this a calibration was performed with a second load washer. It was anticipated that the relationship would vary slightly because as the bone chips become more impacted their stiffness would increase and hence the force at the base of the impactor would change.

A second load washer was mounted in a proximal impactor, see Figure 3.18. A second charge amplifier was acquired enabling readings to be stored in the labview program from both load washers simultaneously. Unfortunately the data acquisition card can only go at 50 kHz when processing two channels, rather than 200 kHz. This reduced the accuracy of these measurements. The hammer was used in conjunction with the instrumented prosthesis to impact defatted cortical-cancellous ovine graft into a sawbone. The results showed that the force at the top of the proximal impactor is approximately 29% of that observed by the sensor in the hammer handle (range 25% to 35%).

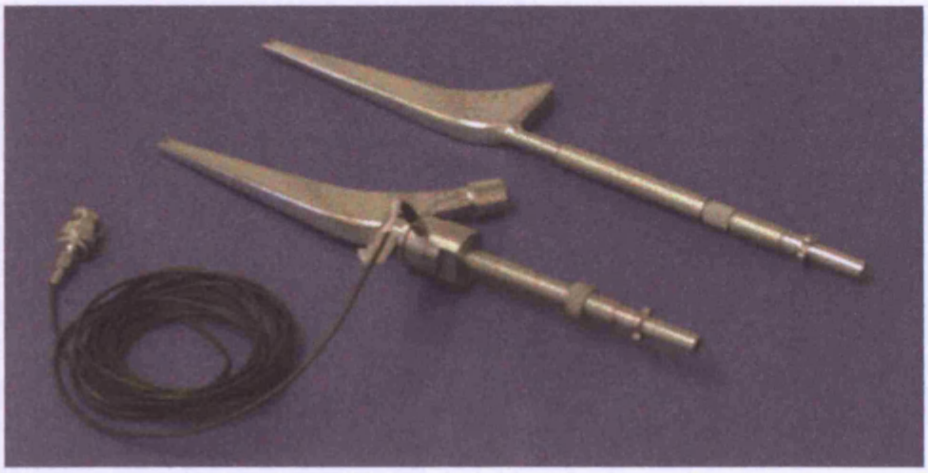

Figure 3.18 - Load washer mounted in proximal impactor

However, later a second laptop and PCMCIA card became available. Now the calibration between the force in the hammer and proximal impactor was repeated with data capture for each load washer at 200 kHz. From ninety-three measurements conducted impacting rinsed human bone chips into a sawbone, the relationship between the force in the impactor was averaged as 0.35 times that of the force in the impactor (SD ± 0.03). The results were calculated for the same measurements using the scale factor of 0.35. The average error by this method was 6 %, with largest error being 20 %. Figure 3.19 gives an example of a force profile measured by the load washer in the hammer and the load washer in the impactor recorded simultaneously. Figure 3.20 shows the relationship between the two. The impaction time of the initial peak is similar for both readings.

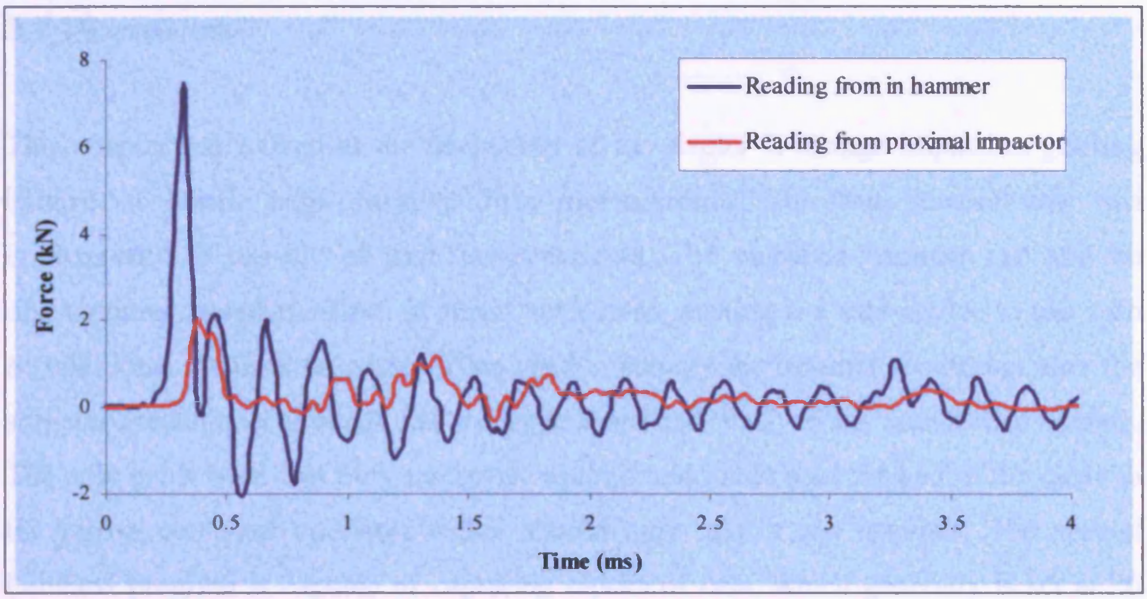

Figure 3.19 - Example of waveforms recorded simultaneously from hammer and impactor

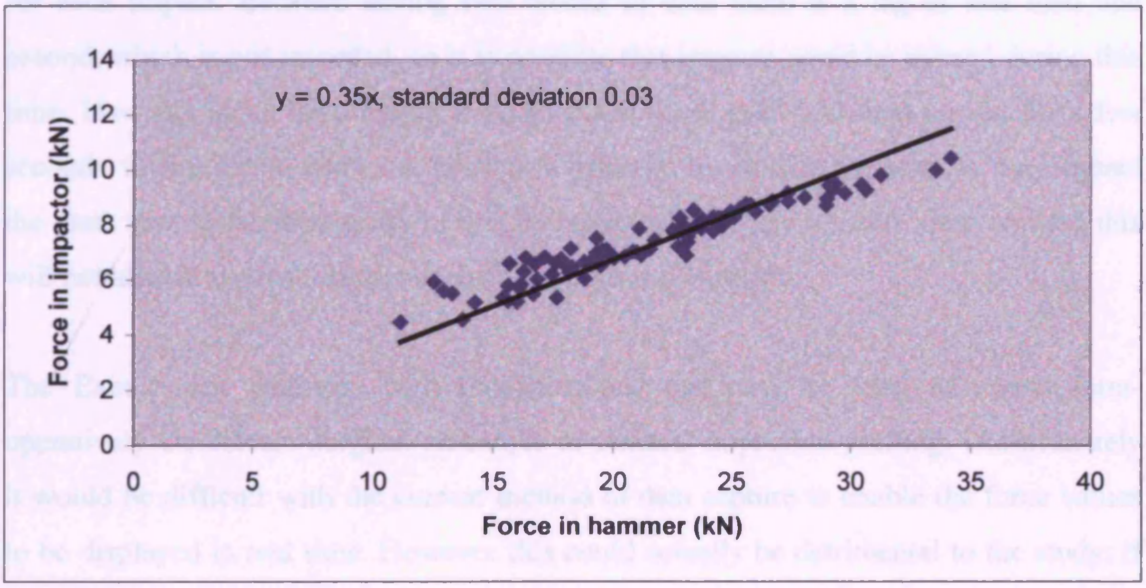

Figure 3.20 - Relationship between force in hammer and force in impactor, measured in an experimental set-up with two load washers

3.7 Discussion

This chapter has looked at the adaptation of the Exeter X-change impaction grafting hammer to enable intra-operative force measurements. The final solution that was implemented is capable of such measurements. The modified hammer can still be decontaminated and sterilised in steam autoclaves, making it a safe device to use with no additional sterilisation costs. When used in surgery the hammer should not alter the surgeon's technique, as it still has the same shape and "feel" of the unmodified version. The only extra work that the surgeon is required to do is to pass the end of the cable to the laptop computer operator, which should only take a few seconds. The special Labview program is capable of capturing blocks of data, which generally is set at 20 seconds. This enables the data to be saved with specific information with regard to the operating procedure, e.g. which impactor is being used and when more bone graft is being added. Once stored it is then possible to filter the data and extract the force values for each impact. Between saving two blocks of data there is a lag of less than one second, which is not recorded, so it is possible that impacts could be missed during this time. However since the surgeon tends to insert some graft and then impact for a few seconds, then pause to add more graft, it is unlikely. In addition the surgeon may impact the graft several hundred times in one operation, so if a few impacts were omitted this will not alter the overall impression of the surgical technique.

The Exeter slap hammer, with modifications, can now be used to assess intra-operatively the current surgical technique of femoral impaction grafting. Unfortunately it would be difficult with the current method of data capture to enable the force values to be displayed in real time. However this could actually be detrimental to the study: if the surgeon was knew instantaneously what forces he was producing, he might alter his technique thereby altering the nature of the proposed study

Calibration of the load washers in the hammer and in the impactor was performed in the Hounsfield testing machine up to a value of 4 kN. However the forces measured in the hammer are likely to exceed 4 kN, so linearity ($<\pm$ 2 % of the load washers range) and hysteresis ($<$ 1 % of the load washers range) of the sensor may create errors in the measured forces. However these errors are small and assuming the forces are in a similar range they will have similar errors making comparisons acceptable. The largest error in analysing the results will occur in converting the forces measured in the hammer to an estimate of those travelling through the impactor. Experiments proved the forces in the impactor are 0.35 times those in the hammer. The average error using this method was 6 % but the largest error was 20 %. The error is probably caused by variations in the inertia of the hammer for each impact, particularly when the stiffness of the impacted material changes.

One of the limitations of the design is the assembly method of the hammer. It is fixed together using a wrench to a preload of nearly 10 kN. However, repeated hammering during an operation could theoretically loosen the device so it must be calibrated between each use. This continual calibration means the hammer will not be able to remain in the hospital sterile services between each operation. Therefore it would be difficult to use the hammer on two consecutive days, however the impaction grafting procedure is not performed routinely. Another limitation of the design is that the force that the surgeon applies to the hammer is measured, not the force that is transmitted to the graft. However calibration with a second load washer has demonstrated that approximately a third of the force measured in the hammer is being transmitted to the impactor. This is because the inertia of the hammer absorbs much of the force. If Stryker Howmedica wished to produce a hammer that did not absorb so much force, it would need to be made from a lighter material than surgical stainless, for example titanium.

3.8 Conclusion

A successful method of measuring the impaction forces in surgery has been developed; this will enable comparisons between operations and variability between several surgeons. The impaction forces measured in the proximal hammer are approximately one third of those in the hammer. Although the forces at the impactor are not equivalent to those in the hammer, they are proportional and are meaningful for other experiments on impaction bone grafting. This study has highlighted that a large proportion of the energy of impaction is driving the weight of the slap hammer.

Chapter 4

Intra-Operative Force Readings During Femoral Impaction Grafting Surgery

4.1 Introduction

The surgeon's technique for crushing the bone chips into place, during impaction grafting surgery, is essentially an undetermined variable. To conduct experiments that proved meaningful results, which can be extrapolated to clinical practice, the surgeon's technique must be quantified and applied back to in-vivo experiments. Brewster at el (1999) used a "standard compaction energy", which they estimated by performing the impaction grafting procedure in a plastic femur and using a force plate to measure the force. Unfortunately, a more detailed description of their set up was not given and the actual values were not disclosed. Wallace et al (1997) also used force plate studies to determine an appropriate load. In their article this is stated as 3.6 N, which is extremely low, although it is possible that there was a typing error and it should have read 3.6 kN. Tanabe et al (1999) decided to impact cylinders containing morsellised bone (diameter 10 mm, height 10 mm) with strikes of approximately 4.2 kN, 15 or 30 times; they chose this set up following the recommendations of Wakui et al (1998). In another series of studies a 455 g weight was allowed to free fall one meter to impact graft into a cylinder of approximately 15 mm diameter and 20 mm heigh, which was intended to "simulate the classical impaction instrument" (Bavadekar et al, 2001; Cornu et al, 2001). This would relate to a momentum of 2.02 Ns, the number of impacts varied between 100 and 150. Voor et al (2000) used a 885 g mass dropped 10 times from 30 cm to impact graft into a cylinder with a height of 76.2 mm and a diameter of 32.3 mm. This would equate to a similar momentum value of 2.15 Ns. However Voor et al (2000) used a much larger volume of morsellised graft and far fewer impactions compared to Bavadekar et al, (2001) and Cornu et al (2001). Kuiper et al (1996) inserted samples into a tube using impulses of 10.3 Ns, which they believed to replicate the average surgical impaction. Unfortunately they do not describe how the impulses were created. All of these studies vary in their prediction of the force, momentum and number of impacts, making it hard to judge how meaningful they are and to compare the results.

The purpose of this part of my PhD was to quantify the current technique of femoral impaction allografting by measuring the forces used, allowing an estimation of the variability that occurs between different patient cases and different surgeons. In addition to the usefulness for in-vivo and in-vitro studies, evaluation of the current surgical technique and its variability will also be extremely constructive for surgeons in clinical practice. This study was conducted using the Exeter slap hammer modified to enable intra-operative force readings as described in Chapter 3. Over a period of one year (February 02 to January 03) nine sets of measurements were recorded during operations by four different surgeons. Any available postoperative radiographs and pain and function scores have also been examined. This chapter details the findings from surgery and patient follow-ups.

The patient follow-ups of this project were conducted with the help of Joyti Saksina.

4.2 Methodology

The enhanced Exeter slap hammer with piezo-electric load washer, described in Chapter 3, was used for this study. Prior to each operation the hammer calibration was checked in the Hounsfield loading machine (Figure 4.1), following the method described in section 3.4d (Static calibration of the load washer). It was then delivered, the day before surgery, to the hospital sterilisation department for autoclaving. Prior to its first use the hammer was decontaminated in 10% decon 90 and distilled water in an ultrasonic water bath. Thereafter a decontamination certificate from the previous use accompanied the hammer when taking it for sterilisation. Patient consent for the measurements was obtained with the surgical patient consent prior to the operation. Measurements were taken at the following hospitals; RNOH Stanmore, Whittington, Princess Grace, Central Middlesex, University Hospital Amsterdam and the "home of femoral impaction grafting," Exeter.

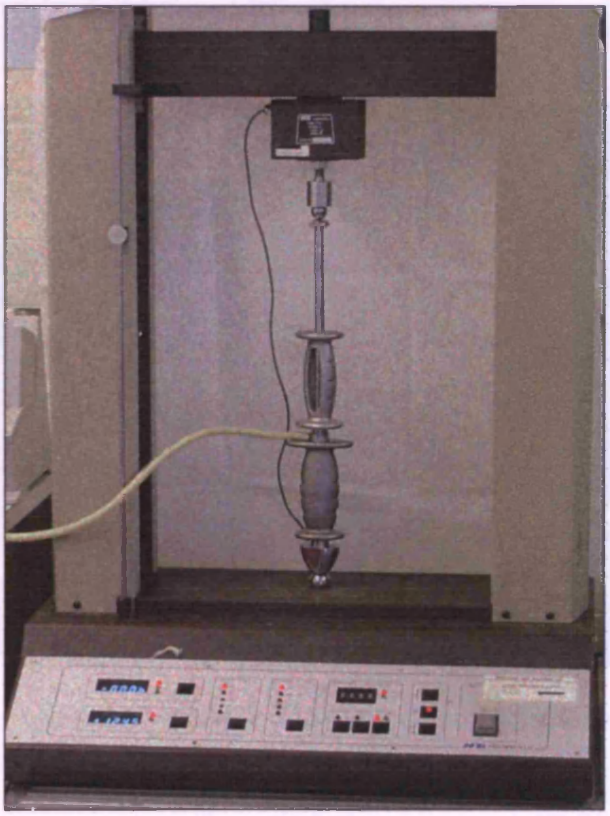

Figure 4.1 – Calibrating the hammer prior to surgery

At the start of an operation the laptop and charge amplifier were set up on a surgical trolley next to an appropriate electrical socket. When the surgeon was ready to start pushing the bone chips down the femur, he took the hammer and passed over the end of its cable. The special sealing cap was removed from the end of the cable (Figure 4.2) so that it could be plugged into to the charge amplifier, which was already connected to the Laptop computer via the PCMCIA card (Figure 4.3). Before data capturing commenced the values on the labview program and charge amplifier were checked as follows:

Labview Program:	Total number of samples	4000000
	Sample rate	200000
	Device calibration (N/v)	4000
Charge Amplifier:	Time Constant	Medium
	Calibration (N/v)	4000

The reason for these values is set out in more detail in Chapter 3.

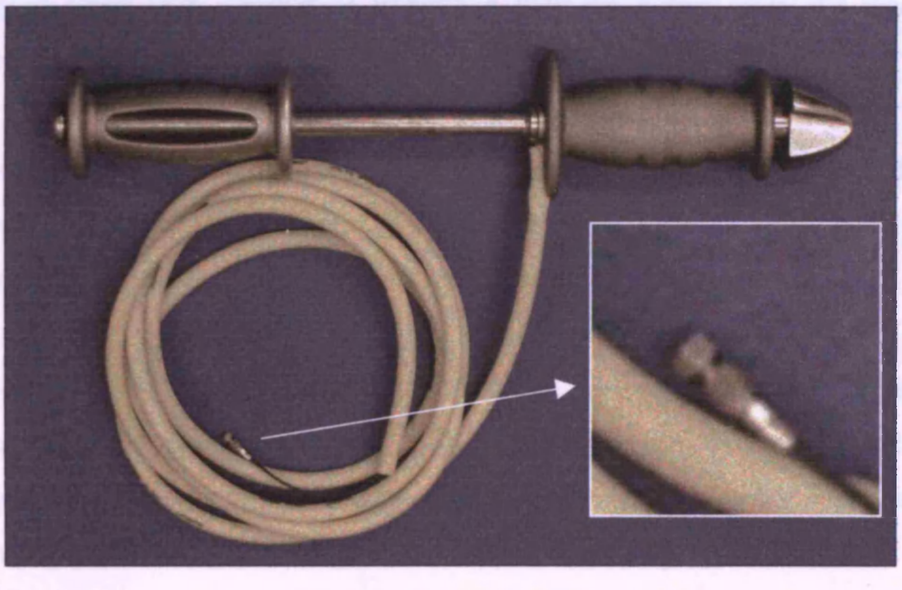

Figure 4.2 - Modified hammer with sealing cap

Figure 4.3 - Charge amplifier and Laptop computer

Once the load washer cable from the hammer had been connected to the amplifier, the reset/operate button (on the amplifier) had to be turned on, which sets the load washer to zero and enables measurements. The range of amplifier is ± 10 volts, so with the range set as 4000 N/v this enabled measurements of ± 40 kN, which was considered large enough. If set at a higher range, any errors in the measurements would be magnified. The surgeon could then commence impaction with the output from the load washer being recorded.

As the surgeon hammered the graft down the femur, the forces ware recorded in 20 second batches (4000000 data points, file size 7.8 Mega Bytes). A reference note was taken to record the impactor being used with the saved labview file name.

Once the surgery was finished, the sealing cap was firmly screwed into the end of the cable and then the hammer was left for decontamination with the other surgical instruments. The hammer was normally collected, with an appropriate decontamination certificate, from the sterilisation department the day after surgery.

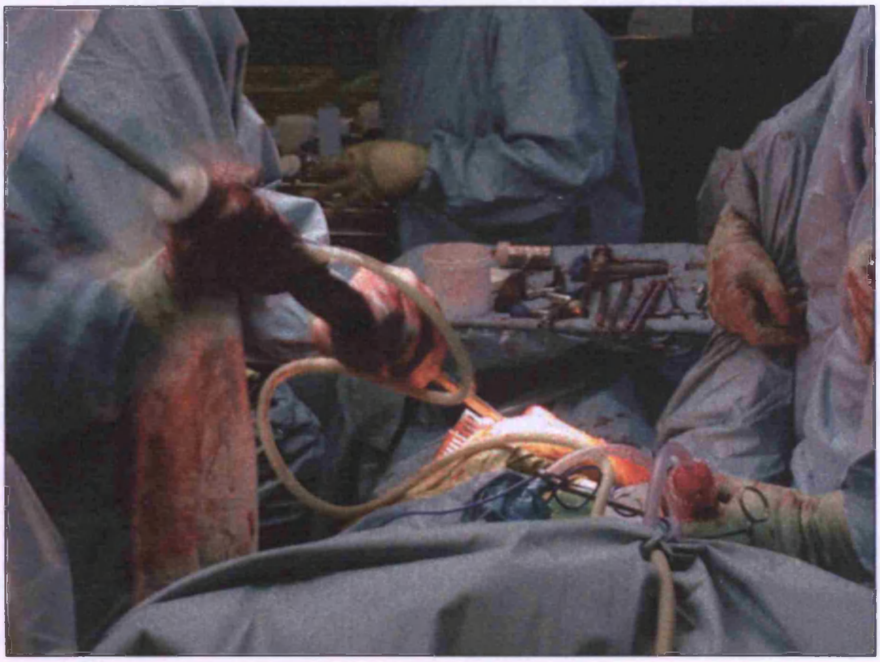

Figure 4.4 - Using the modified Exeter hammer to impact bone graft in femoral revision surgery

Figure 4.4 shows the hammer being used during an operation. The postoperative weight bearing of each patient was left to the discretion of the surgeon, and varied between six weeks and three months. The bone loss was graded using the AAOS classification system (D'Antonio et al, 1993), a description of this can be found in the Literary Review Chapter of this thesis (2.3a Surgical Technique). Postoperative pain and function were assessed using the Harris Hip Score (HHS). Gross subsidence was measured using pre and postoperative radiographs following the method described by Eldridge et al (1997). A reference line was drawn down the long axis of the femur. Another two lines were then drawn perpendicular to this, one through centre of rotation of the femoral head and the other to a reference point on the femur. The reference point was either the tip of the greater trochanter, the medial neck or tip of the lesser trochanter, depending on which was clearest on the radiographs.

4.3 Results

The hammer was easy to use in surgery and did not interfere with the surgeon's usual technique. During two of the operations the charge amplifier flashed overload error, indicating the signal had exceeded 10 volts, because the surgeon had generated a force in excess on 40 kN. Subsequently the range in the amplifier and labview program were changed to 6000 N/v (allowing measurements to 60 kN), and the reset/operate button was turned off and on again to reset the amplifier before measurements were recommenced.

The force profiles recorded in surgery were similar to those conducted in preliminary laboratory tests. There was a distinct initial peak representing the force, followed by a period of oscillation, which is inherent with metal hitting metal. Experiments described in Chapter 2 have shown that the force in the proximal impactor is approximately 0.35 times (SD ± 0.03) that observed by the load washer in the hammer. The profile of impaction for both measuring points was similar, with matching impulse times, which implies that the momentum in the impactor is also approximately 0.35 times lower than that in the hammer. Table 4.1 shows the distal and proximal forces measured using the modified hammer in surgery. The average force readings from all the cases ranged from **6.1 to 28.9 kN**, which equates to **1.8 to 8.4 kN** in proximal impactor. Figure 4.5 and Figure 4.6 give examples of force profiles during distal and proximal impaction of case A/3. The force profile of each impact lasts for approximately 0.15 ms. Even with the larger forces experienced during the proximal impaction of case C/7 the impulse time was still about 0.15 ms (Figure 4.7). The area under the graph should equate to the momentum of impaction and can be estimated using a triangle. This implies that a 6.1 kN impact measured in the hammer would have a momentum of 0.46 Ns, and a 28.9 kN force would have 2.17 Ns. However these figures still have to be multiplied by 0.35 to obtain momentum values of **0.16 Ns** and **0.76 Ns** in the impactors. Surgeon C created some impacts with force readings above 60 kN. These readings will have larger errors as they are outside the measuring range of the load washer, however they would imply momentum values of approximately 1.58 Ns in the impactors.

Surgeon / Patient	Opp. Date	AAOS	No. Distal impacts	Mean ± SD distal force (kN)	No. Prox. impacts	Mean ± SD prox. force (kN)
A / 1	26/2/02	III	27	8.8 ± 2.0	90	24.5 ± 5.8
A / 2	5/3/03	IA	25	14.1 ± 5.2	152	17.1 ± 3.1
A / 3	18/6/02	IB	45	15.4 ± 2.1	61	20.3 ± 8.9
A / 4	24/4/03	IA			256	18.1 ± 4.7
A / 5	12/5/03				126	20.2 ± 6.0
B / 6	20/3/02		293	21.8 ± 7.2		
C / 7	31/10/02		153	17.4 ± 7.7	489	23.2 ± 9.5
C / 8	7/11/02		41	17.8 ± 7.0	173	28.9 ± 11.3
D / 9	28/1/03	III	116	8.1 ± 5.4	129	6.1 ± 2.8

Table 4.1 - Forces measured during nine operations

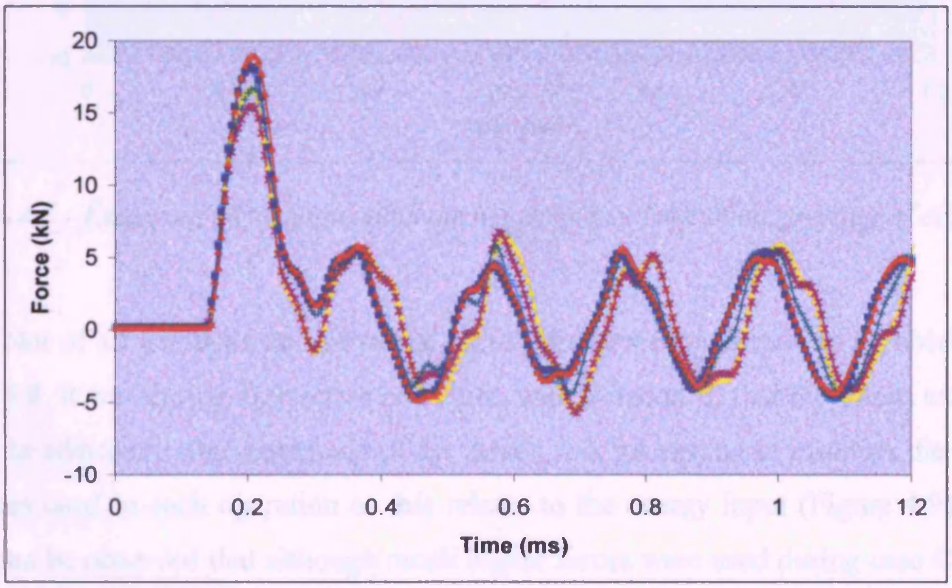

Figure 4.5 - Examples of force profiles during distal impaction grafting of case A/3

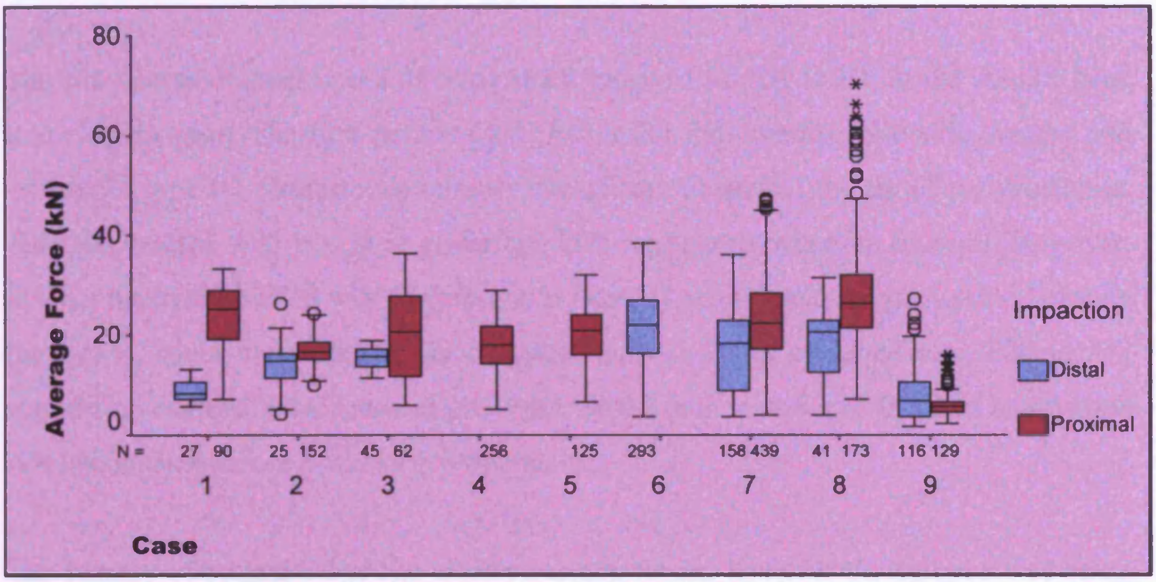

Figure 4.8 - Box plot of intra-operative force measurements

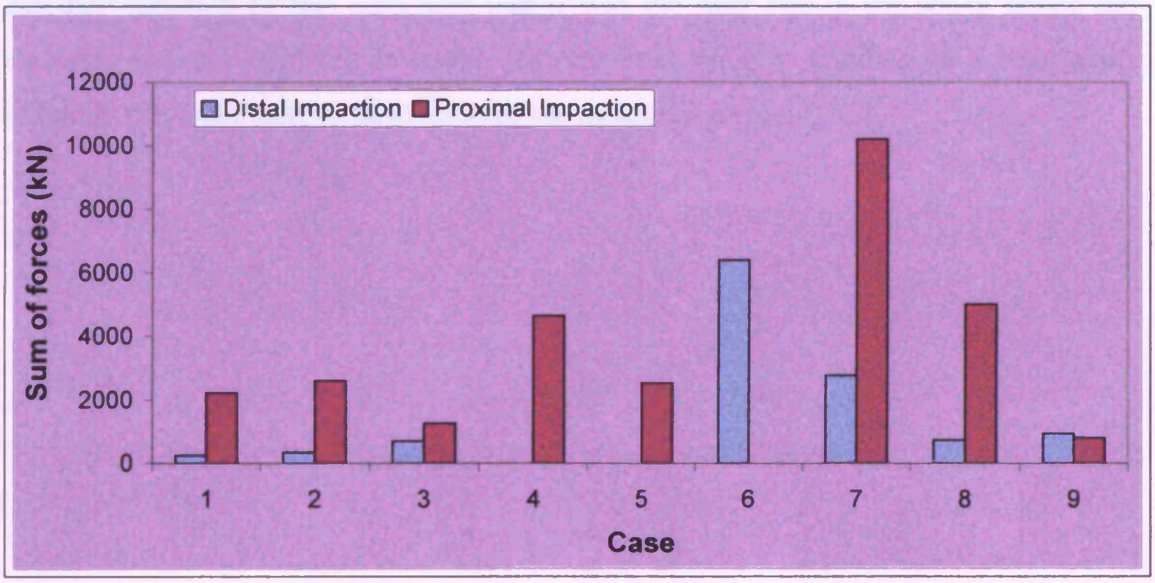

Figure 4.9 - Graph illustrating the sum of forces for each case

Of the five cases with surgeon A, two involved only light hand tapping for the distal impaction, which was not measured. Case B/6 was a long stem impaction with severe bone stock loss. Consequently the surgeon used high distal impaction, but proximally the bone was very weak and required a large mesh, so only light proximal impaction was performed which was not recorded. Measurements in a further two cases of surgeon C were attempted, but unfortunately the high forces from this surgeon caused the hammer to loosen, rendering the results invalid.

The pre-operative assessment of bone stock ranged from IA to III on the AAOS bone loss classification. The first patient (A/1) had a fall five months following surgery and suffered a type B1 fracture (Vancouver classification) around the tip of the prosthesis. This was treated with two strut grafts and OP1 ten months after the fracture. However, at three months the HHS was 58 (pre-opp it was 24) and showed no gross subsidence on the x-rays, while measurements at one year showed 2 mm of subsidence. Patient A/2 showed no marked subsidence at one year, whilst patient A/3 had 0.5 mm and patient A/4 had no subsidence 6 weeks postoperative.

The surgery of patient 9 had the lowest average forces, however the surgeon was being cautious as he had a Grade III cortical deficiency (AAOS classification). Three months postoperative HHS has improved from 52 to 74 and there is no observer subsidence. Another variation of this case was that it was the only one in the series where the cartilage was not removed from the femoral head prior to grinding in a bone mill, although this is unlikely to have affected the measured forces.

4.4 Discussion

The impaction forces have been measured during nine operations performed by four different surgeons. The study shows variability between surgeons and variability between patients operated on by the same surgeon. More cases need to be undertaken to observe any real trend between the impaction forces and the patient's outcome. The lowest forces observed in this study have so far not been associated with migration.

The average force readings range from 6.1 to 28.9 kN, which equates to 1.8 to 8.4 kN in proximal impactor. Tanabe's value of 4.2 kN lies in the middle of this range. The estimated momentum in the impactors for that force range would be 0.16 Ns to 0.76 Ns, less than half the values calculated for the apparatus described by Bavadekar et al (2001), Cornu et al (2001) and Voor et al (2000), and a tenth of that used by Kuiper et al (1996). However, the momentum values are only an approximation of the area under the force time graph and as such may be underestimated. Also some higher forces were observed with momentum approximations of 1.58 Ns, but these were very rare and did not represent the majority of impacts.

Experimentally impact forces are normally produced by dropping a weight a specified distance and for this set up, the momentum can be calculated. In surgery the forces are produced using a weight and the surgeon's strength. Consequently it is not possible to calculate the momentum, although it can be derived from a measured force time profile. It is possible that an identical peak force created by these two methods will have different momentum values.

The number of impacts used to impact distally ranged a great deal, from 25 to 293. However, the case with 295 impacts was a long stem with severe loss of bone stock, hence the high number of distal impacts. The range could be due to variations in bone stock, but could also be due to the choice of the surgeon to do more of the distal impaction by hand. In a few of the published experimental studies, graft is impacted into cylinders (Tanabe et al, 1999; Bavadekar et al, 2001; Cornu et al, 2001; Voor et al, 2000), which could be likened to the distal impaction in the shaft of a femur. Consequently for cylindrical impaction studies, in particular those with diameters similar to the internal femur shaft (10 - 15 mm), a range of 25 to 150 impacts can be recommended to replicate the surgical procedure.

The range in the number of proximal impacts was even larger than distally; 61 to 489. Again this may have been related to the size of cavity filled, as well as the surgeon's technique. Adding all the forces together gives an indication of the variation in energy used between operations, and highlighted that the case with the highest force did not correspond with the largest energy input, but was actually similar to a case where lower forces had been used. The total energy of an operation should ideally be related to the graft volume used, unfortunately the graft volume was not measured. The magnitude of the force only becomes more important than the energy if it must exceed the yield point of the graft particles. That is to say, it is necessary for optimum impaction that the graft particles suffer permanent deformation, i.e. they fracture and interlock. The investigation of the yield point of the bone chips and the relationship with the surgeons applied force is a possible area for future research.

The average readings in this study show that the forces travelling through the impactor range between 3 to 11 times body weight. Bergmann et al (1993) found that the forces through a hip prosthesis are in the range of 2.8 to 5.5 times body weight for walking and jogging, but can rise to nearly 9 times body weight with stumbling. This implies that the impaction forces are not considerably larger than those which will be experienced post operatively, particularly considering the fact that the force profiles during walking last approximately one second, far longer than the 1.5 ms of the impact force. It is therefore possible that the subsidence observed postoperatively, following an impaction grafting procedure, are a result of further compaction of the graft from the pressures created during walking.

The work of this study has tested the developed measurement system of impaction forces. The system has been found capable of performing its designated task, although loosening of the load washer in the hammer does appear to be a problem under height forces. To remove this problem the adaptation of the hammer would need further work, it might be possible to weld the preloaded washer in situ. However, the heat from welding could damage the load washer, and such an assembly would be hard to undo if the preloading bolt stretched or if the load washer became damaged. A point that was also highlighted during the analysis of results was that to determine the impulse time and the momentum, each impact had to be plotted. It might be possible to develop the labview program further to include evaluation of impulse time and momentum during processing.

4.5 Conclusion

A successful method of measuring the impaction forces in surgery has been developed. Problems with this device arise when excessive forces are used causing the hammer to loosen. This would be difficult to overcome in the current modification set up.

The study shows variability between surgeons and variability between patients operated on by the same surgeon. The average distal force readings range from 8.1 to 21.8 kN, which equates to 2.8 to 7.6 kN in the distal impactor. The average proximal force readings range from 6.1 to 28.9 kN, which equates to 1.8 to 8.4 kN in the proximal impactor. These readings show that the forces travelling through the impactor range between three to eleven times body weight and have approximate impulse values of 0.16 Ns and 0.76 Ns. Depending on the nature of the study, I would recommend using forces with values in the middle of these ranges for future research.

Chapter 5

Effect of Different Particle Sizes on Mechanical Strength and Remodelling Rate of Impacted Allograft

5.1 Introduction

A predominant problem in impaction grafting is subsidence of the stem; possible causes of this are under impaction of the bone graft and resorption of the graft during the remodelling process. During a study in bone chambers in rats, Tagil (1998) found that impaction of the graft delays remodelling, which contradicted their hypothesis. They had believed that the greater level of surface area would increase remodelling. In subsequent discussion they suggested that the over impaction of the graft might reduce the space required for revascularisation and remodelling would thereby be inhibited. A high level of impaction of the bone graft is necessary in impaction grafting in order to provide sound stability of the stem and to prevent subsidence. Clinically there have been biopsies and post-mortems showing remodelling of the graft from clinical cases where subsidence has not been a problem; this could indicate that it may be possible to find a middle ground on which there is space for remodelling without threatening the stability. **Rather than varying the level of impaction, it could be beneficial to change the graft size, which would affect the porosity of the impacted structure as well as the graft surface area, thereby altering the revascularisation and remodelling rate.**

There have been several in-vitro studies investigating the effect of graft size on its mechanical stability indicating that larger chips offer improved stability; this was discussed in the Literature Review (Chapter 2). The effect on osteoconductive properties with relation to bone chip size has not previously been investigated. However there are several published in-vivo studies that have looked at the effect of porosity of synthetic bone graft substitutes, such as hydroxyapatite and tricalcium phosphate (again discussed in the Literature Review). In synthetic graft a high porosity and inter connective porosity has been shown to be important; although the optimum pore size still appears to be under debate it would seam that it should be within the range of 150 - 400μm. It is arguable that this could be applicable to impacted bone chips. Assuming the chips do not suffer total crushing, they will have the natural porosity of cancellous bone. However smaller chips are likely to compact to create a large number of interconnecting pores, whereas larger chips will be interspaced with fewer but larger voids.

Brewster et al, (1999) discuss the mechanical advantages of creating a size distributed graft mixture using Soil Mechanics Theory. This "idealised" graft described by

Brewster is designed to have the smallest possible void spaces between the bone particles and may have even lower osteoconductive properties than graft made from a single size range. Griffon et al, (2001) used the "idealised" graft as a positive control in their ovine model, however they did not compare its biological properties with an un-graded allograft sample.

Tagil et al (1998) did not find the positive effect on remodelling that they were anticipating by increasing the overall surface area of the graft through impact the graft, but their bone chamber model was totally unloaded. Indeed the same group went on to prove, in a rabbit tibial tray model, that loading of the graft increases remodelling (Wang et al, 2000). However the bone chamber in Tagil's study was only 2 mm diameter and 7 mm deep, so the graft must have been very small. For Wang's study, chips of 1 to 1.5 mm were used which is still a lot smaller than used in human surgery. Griffon et al (2001) describe an ovine model for investigating graft with a 15 mm diameter defect, 15 mm deep, in the distal femur and proximal tibia. These sites are within cancellous bone and, although they will not be subjected to the high loads of a hemi arthroplasty model, more load will be applied to the graft than in a bone chamber, and the defects would be large enough to test graft size of clinical relevance.

Consequently the study described in this chapter investigated the remodelling rates of Small, Large and Graded graft sizes in an ovine model similar to Griffon at al (2001), with an empty site as a negative control. Four graft sites were selected; the medial aspect of both distal femurs and proximal tibias. In Griffon's study they used the lateral side of the distal femur, however examination of a bone found the medial side to be much flatter, so easier to fix a guide plate to. The medial approach was chosen for the defects in the femur and tibia. Ten sheep were used, with the intention of euthanising half the group at six weeks and the remainder at twelve weeks.

In conjunction with the in-vivo analysis, the different grafts were investigated for their mechanical stiffness during stages of impaction following a similar procedure to that described by Bavadekar (2001). The impacted grafts were embedded in resin and sectioned to allow quantification of the porosity of the graft types.

Hypothesis

The impacted small graft chips will have the best remodelling due to the osteoinductive properties of a large fracture surface area and osteoconductive properties of the large number of pores. Although the graded graft mixture will have similar osteoinductive properties to the small graft, the close packing of its impacted structure may inhibit remodelling. The large graft may have lower osteoinductive and osteoconductive properties compared to the small graft.

5.2 Methodology

This part of the thesis was conducted in two halves; one part tested, in-vitro, the mechanical properties of three different grafts (termed Small, Large and Graded) at time zero. The other part investigated, in an in-vivo ovine model, the rate of remodelling of the graft types.

5.2a Preparation washed morsellised graft

Bone graft for the mechanical and in-vitro study was prepared using an identical protocol, and was designed to produce an ovine version of the fresh frozen defatted human allograft that can be purchased from bone banks. This optimises the graft properties by cutting off the cartilage and removing the fat through multiple washes. De-fatting the graft improves its mechanical and biological properties (van der Donk et al, 2003).

For the mechanical experiments the bones came from a butcher, but to ensure freshness for the in-vivo study the bones were collected from an abattoir the day after slaughter. The bone graft was prepared from ends of femora and humeri, and the proximal end of tibias. These areas were chosen for their high quantities of cancellous bone.

The graft was prepared in a similar manner to the North London Tissue Bank (NLTB)[1] protocol for creating their Ground Frozen Irradiated Bone Graft. The bones were stripped of any tissue and cartilage before they were morsellised in the Lere bone mill[2]. To enable the bones to fit down the 25 mm diameter tube of the bone mill they were first cut into small sections using a bandsaw[3]. The washing of the graft was almost identical to the NLTB protocol except that the 3% Hydrogen Peroxide wash was omitted, since this is included predominantly for aesthetic purposes. The protocol is set out in Table 5.1. As no shaker was available, the graft was stirred and swilled during some washes. The temperature of the water (~ 55 °C) used to wash the graft was measured with a thermometer. Once the graft has been washed, excess water was soaked up using paper towels.

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[1] North London Tissue Bank, Deansbrook Road, Edgeware, Middlesex, HA8 9BD

[2] DePuy, St. Anthonys Rd, Beeston, Leeds, LS11 8DT

[3] Draper

Step	
1	1 × Sonic water wash 15 minutes @ ~55°C
2 - 4	3 × Stirred water wash 15 minutes @ ~55°C
5	1 × Stirred water wash 60 minutes @ ~55°C
6	1 × Stirred 70% Alcohol 10 minutes sonic wash
7 - 8	2 × Stirred water wash 15 minutes @ ~55°C

Table 5.1 - Protocol for washing the morsellised graft

5.2b Creating the graft groups

Three different graft groups were used in this study, Large, Small and Graded groups. The Large group consisted of particles in the size range of 6.68 - 4.76 mm and the Small group from 3.20 - 2.00 mm, these ranges were chosen to replicate extremes currently used in surgery. The Graded group was chosen to replicate the idealised graft used by Brewster et al (1999) and Griffon (2001) using the optimal curve for irregular shapes. The graft was sieved in a shaker for an hour, to produce a range of sizes from 1 mm chips up to pieces over 10mm. The shaker used was from the Civil Engineering Department at UCL and the sieve sizes, which gave the graft size range, were 1, 2, 3.2, 4.75, 6.68 and 9.42 mm. To produce graft pieces of under 1 mm for the "idealised sample" some graft was then passed through a Waring blender to produce extra fine graft, which was separated with 0.5 and 0.1 mm sieves. The graded graft was created by mixing the required weight ratios from each size band (Table 5.2). Figure 5.1 shows the optimal curve for irregular shaped particles taken from Brewster et al (1999) (A) and a graph of the Graded graft used in this study (B).

Size (mm)	Distribution of graded graft by weight
9.42 < 6.68	9 %
6.68 < 4.76 (large graft)	11 %
4.76 < 3.20	13 %
3.20 < 2.00 (small graft)	13 %
2.00 < 1.00	22 %
1.00 < 0.50	12 %
0.50 < 0.10	20 %

Table 5.2 – Graded graft size distribution

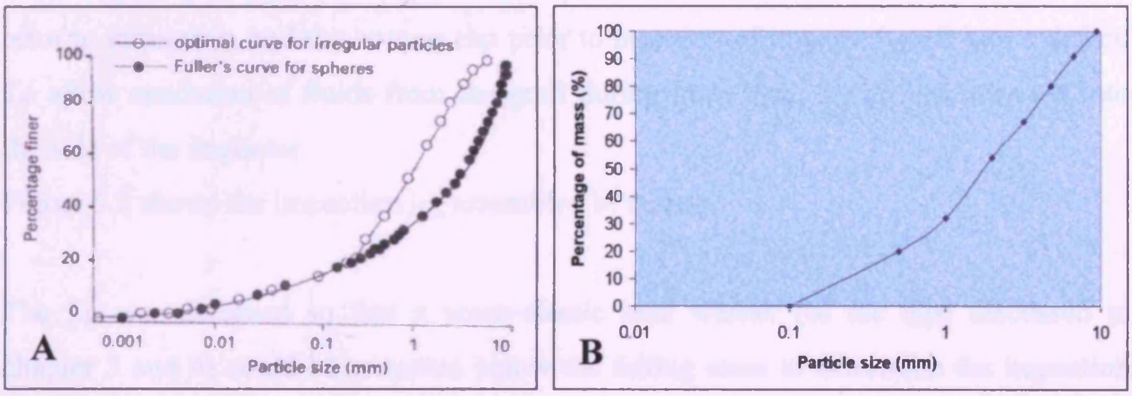

Figure 5.1 - (A) Graph of optimal curve for irregular shapes, taken from Brewster et al (1999), (B) Graph of Graded graft from my study

5.2c Irradiating the graft

It was not possible to prepare the graft aseptically, so irradiation was chosen as the sterilisation method for the graft in the in-vivo study. Currently much of the graft used clinically is irradiated. However the graft for the mechanical study did not undergo irradiation. The graft in each group was thoroughly mixed then placed as 5 gram samples in individual cylinders with lids. These were then double packed in airtight plastic bags and frozen at –70 °C. The samples were sterilised by gamma irradiation with a dose of between 30 and 35 KGrays (Isotron, Reading, UK), and stored at –20 °C until surgery, when it was defrosted for two hours prior to surgery.

5.2d Impaction Jig

A dual-purpose impaction jig was designed for the study to impact bone graft into 15mm diameter cylinders. For the mechanical study it was mounted in the Dartec loading machine, whilst for the in-vivo study it was sterilized in an autoclave and assembled in an aseptic manner in the operating theatre. A pair of callipers attached to the jig measured the height of the graft during impaction. For mechanical testing, digital vernier callipers accurate to a tenth of a millimetre were used. However, these could not be autoclaved, so in the surgical setting stainless steel vernier callipers were used, as only the final impacted height was required. These were readable to a quarter of a millimetre. The impactor was designed to impact graft into Tufnol®[1] cylinders with an outer diameter of 20 mm and an inner diameter of 15 mm, Tufnol® was used as it has similar mechanical stiffness to bone (E = 6.9 GPa). The Tufnol® tubes were capped at both ends so that the graft could be sterilised in the tube, the top cap being removed prior to impaction, and the bottom cap prior to insertion of impacted graft into a defect. To allow exudation of fluids from the graft during impaction, six groves were cut into the side of the impactor.

Figure 5.2 shows the impaction jig assembled in theatre.

The jig was designed so that a peizo-electic load washer (of the type discussed in chapter 3 and 4) could be mounted below the falling mass to determine the impaction force. A five gram sample of bone chips was impacted by dropping the 1 kg mass from various heights and the impact force recorded. This was repeated with a further nineteen samples to produce a curve of drop height against resultant force for the impaction jig (Figure 5.3) Unfortunately the data on surgical forces in Chapter 4 had not been collected at the time this study started. Therefore the impaction force had to be determined from the literature. The mechanical testing part of this study is similar to that of Bavadekar et al (2001) and Cornu et al (2001), so it was decided that a similar impaction process should be used. In their studies a weight of 455 g was allowed to fall one meter at least a hundred times to impact graft into a cylinder of 15 mm diameter. The momentum of such an impact would be 2.02 Ns. To produce a comparable impact, the one kilogram mass of the impactor jig was allowed to free fall 20 cm, equating to a momentum of 1.98 Ns. When measured with the load washer this was found to equate

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[1] RS Green Lane, The Fairway Estate, Hounslow, Middlesex, TW6BU

to a force of approximately 15kN. To have the largest effect on the porosity it was decided that each sample should be subjected to one hundred impacts.

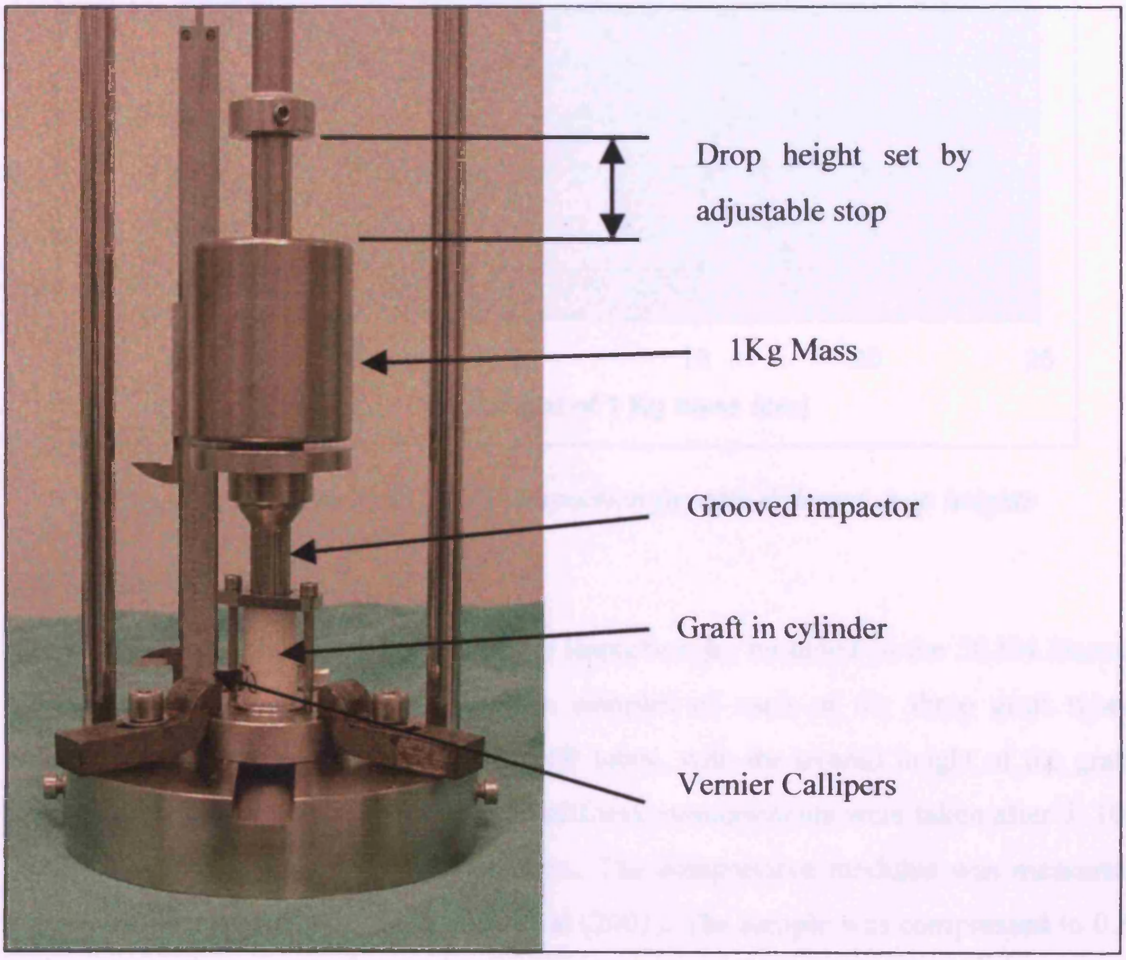

Figure 5.2 - Impaction jig set up in surgery

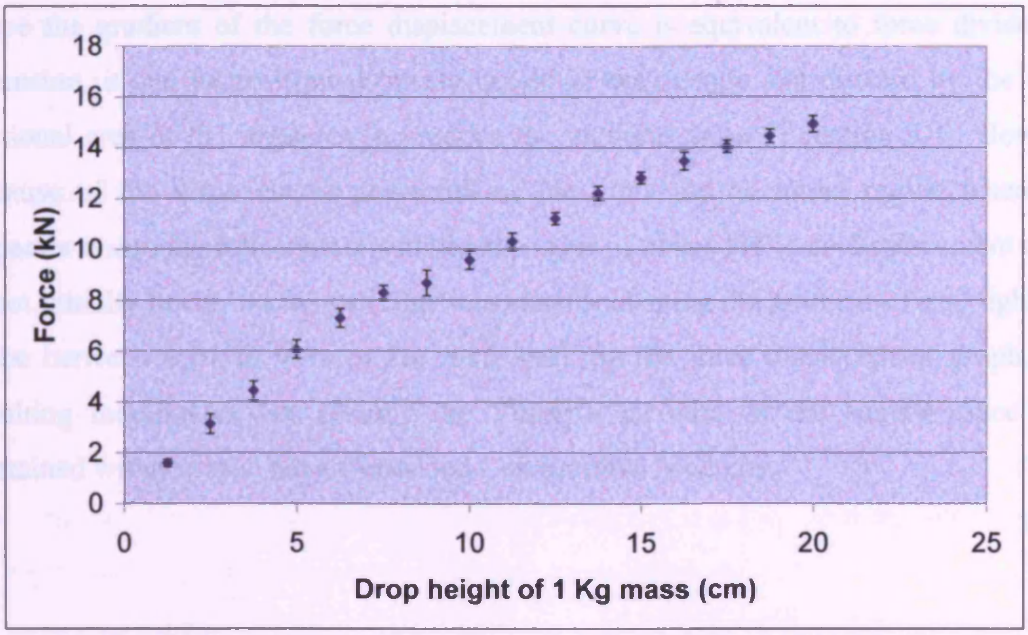

Figure 5.3 - Force measured in impaction jig with different drop heights

5.2e Mechanical tests

Mechanical tests were performed with the impaction jig mounted in the 50 kN Dartec hydraulic loading machine[1]. Six 5 gram samples of each of the three graft types underwent one hundred impacts in Tufnol® tubes, with the overall height of the graft recorded after each impact. Compressive stiffness measurements were taken after 5, 10, 15, 20, 30, 40, 50, 60, 80 and 100 impacts. The compressive modulus was measured using a similar technique to Bavadekar et al (2001). The sample was compressed to 0.3 mm at a rate of 0.5 mm/minute, and the load was then released.

The modulus of elasticity, E, (also known as the Young's Modulus) is used to describe the stiffness of a material prior to yield in tension or compression, and is calculated as the ratio of unit stress to unit strain within the proportional limit of the material (Equation 5.1).

	$\mathbf{E = \sigma/\varepsilon}$	(Stiffness = stress / stain)	*Equation 5.1*
	$\mathbf{\sigma = F/A}$	(stress = force / area)	*Equation 5.2*
	$\mathbf{\varepsilon = ext/oL}$	(stain = extension / original length)	*Equation 5.3*
Hence	$\mathbf{E = (F/ext) \times (oL/A)}$		*Equation 5.4*

[1] Dartec HA50, Zwick Roell Ltd, Uk

Since the gradient of the force displacement curve is equivalent to force divided by extension, it can be multiplied by the height of the sample and divided by the cross sectional area of the impactor to produce the modulus value (Equation 5.4). However because of the visco elastic properties of the graft and an initial region where the impactor is coming into contact with the top layer of chips, the force displacement curve is not initially linear. So the modulus was calculated using the gradient of a straight line to be between 60% to 98% of the final load, on the force displacement graph. The resulting modulus is not actually the Young's modulus of the sample since it is contained within a tube but a Contained Compressive Modulus.

5.2f In-vivo testing

Ten adult female mules (body weight varying from 60 kg to 85 kg, with mean and standard error of mean 70.7 ± 7.1) were used during this study. Five sheep were terminated at six weeks and five at twelve weeks. The test areas were: medial, distal femur and proximal medial tibia on both hind legs. Allocation of the four types (Small, Large and Graded graft plus an empty control) was done using the Latin square design. However several days after surgery the first two sheep appeared to still be in discomfort and coupled with the fact that there were concerns of fracturing around the empty site, it was decided that the remaining sheep would not have a hole drilled in the empty site.

To assist the surgery tibial and femoral guide plates were made, both of which could be fixed into position using 2.7 x 18 mm sized self tapping bone screws. To create the hole 5, 10 and 15 mm diameter drill guides could then be mounted into a recess in the plates. This recess also accommodated the Tufnol® cylinders containing the pre-impacted graft.

All the surgical procedures (including the pre and post operative care) conformed to the Animals (Scientific Procedures) Act 1986 and were carried out by either Mr Mahmood or Professor Blunn with an anaesthetist. Prior to surgery, a personal licence was obtained by Mr Mahmood from the Home Office (Queen Ann's Gate, London), under the project licence of the Professor Blunn (project supervisor). During the surgery I set up the sterilised jig and impacted the graft in the cylinders.

Forty-eight hours prior to surgery the animals were individually housed in pens and 12 hours prior to surgery they were starved but allowed to drink. Premedication (Xylazine HCl solution 2% at 0.2 mg/kg, intramuscular, Bayer PLC, Germany) was administered half-an-hour prior to administration of anaesthesia in the preparation room. Anaesthesia was induced with intravenous injection of Hypnovel® (midazolam 2.5mg stat dose, Roche Products, UK) in left jugular vein. Anaesthesia was maintained by inhalation with a mixture of Halothane (Meriel Animal Health Ltd) and oxygen delivered by an endotracheal tube. Oxygen saturation and pulse were monitored throughout the operation with a pulse oximeter. The fleece over a large area on the anteromedial aspect of each knee was clipped and the wool removed. The skin was washed thoroughly with Iodine-Povidine solution diluted in water. The animal was then moved to operating theatre. The wound site was further cleaned with Chlorhexidine. Sterile drapes were used to isolate each knee in turn. Prophylactic antibiotic (Ceftiofur - Pharmacia, Northampton, UK) and analgesics (Buprenorphine 10-20 μg/kg, Reckitt and Coleman Products, UK) were given intramuscularly at induction.

The medial femoral condyle was approached through a 40 mm medial incision based just proximal to knee joint, along the shaft of femur and 30 mm posterior to the patella trochlar groove. The vastus medialis was split along the line of its fibres. The periosteum was lifted from the bone surface. The femoral guide plate was fixed in position using the bone screws (Figure 5.4). A defect was created using 5, 10 and 15 mm drill bits, as shown in Figure 5.5 and Figure 5.6, with drill-stop position at the required position (depending on the final height of the impacted bone graft plug). Whilst this was being performed the graft was compressed in the impaction jig. The Tufnol® tube containing the impacted graft plug was then mounted on the guide plate and the plug was gently introduced into the defect using a plastic rod with diameter of 15 mm, Figure 5.7 and Figure 5.8. The graft now in place, the Tufnol® tube and the guide plate were removed. The wound was closed in two layers, with subcuticular stitches for skin closure.

A 40 mm longitudinal incision was made over the medial aspect of proximal tibia just distal to the knee joint line and 20 mm posterior to the tibial tuberosity. The wound was continued through the subdermal fascia onto the bone (proxi-medial tibial metaphysis). Skin and fascia were retracted and haemostasis achieved. Position of the knee joint was confirmed with needle arthrocentesis. Attachment of the tibial guide plate, drilling of the defect, insertion of the graft and closing the wound was performed in the same way as for the femur. The animal was redraped and a similar procedure carried out around the opposite knee joint.

Post-operatively, the animals recovered in individual pens in sternal recumbencey. Prophylactic antibiotic and intramuscular analgesics were continued for three post operative days. One group of animals were euthanased at 6 weeks post surgery, and another at 12 weeks (with intravenous injection of 50 ml of 20% Phenobarbital). After death, the distal half of femora and proximal half of tibiae were carefully harvested through the old incisions. All the muscles, tendons and ligaments were cleaned off the bone, with minimum disruption to the periosteum around the operated sites, and immediately placed in 10% formal saline.

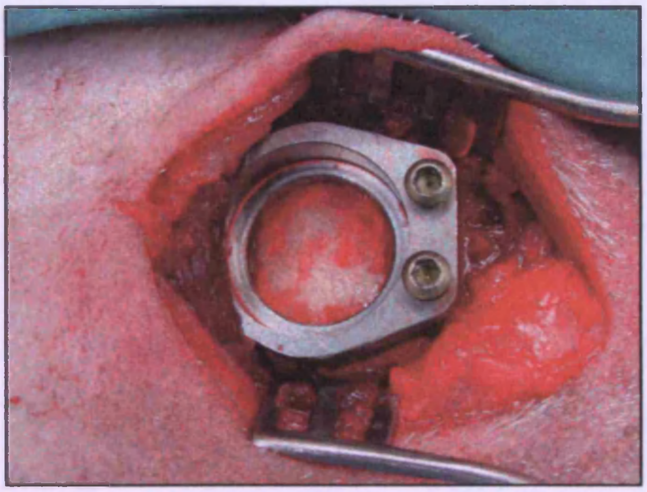

Figure 5.4 - Femoral plate in position

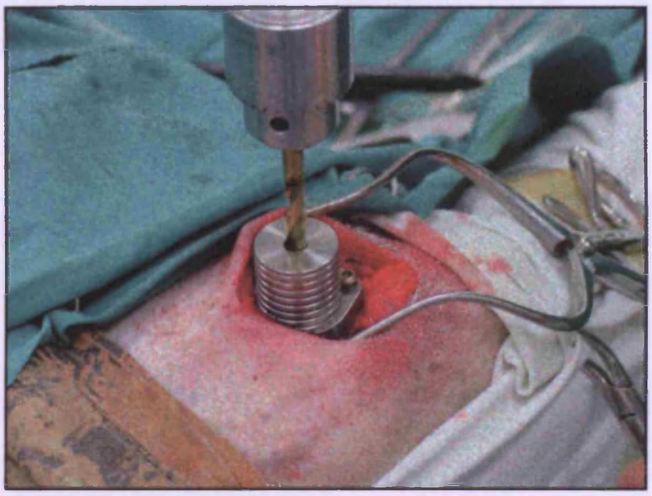

Figure 5.5 - Drilling a 5mm hole

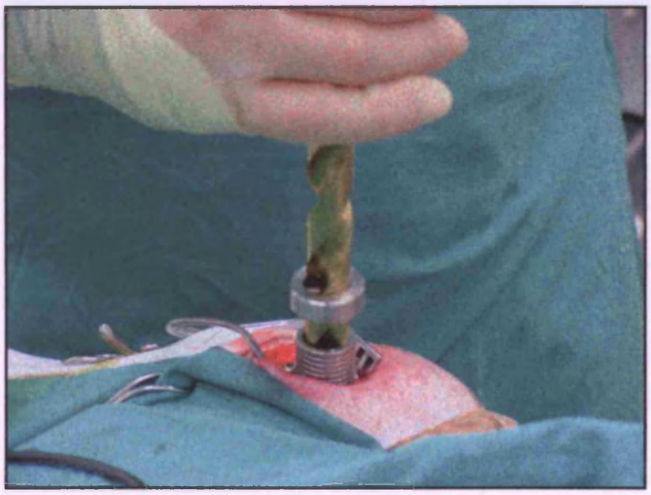

Figure 5.6 - Drilling a 15mm hole with a drill stop

Figure 5.7 - Tapping the graft into the defect

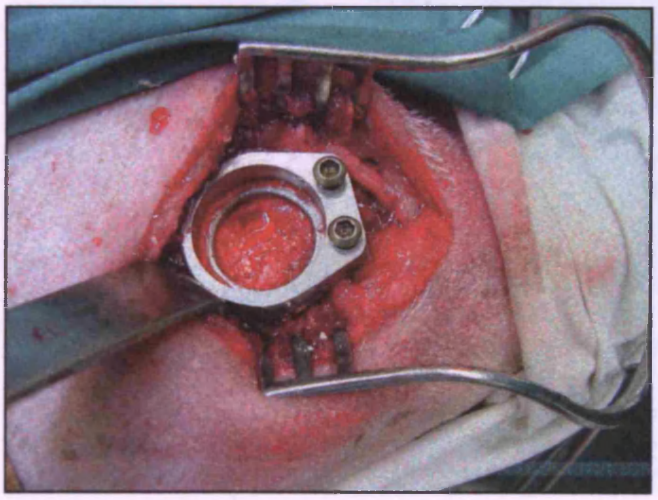

Figure 5.8 - Graft in a femoral defect

5.2g Computer Tomography Scans

Each bone was radiographed in anteroposterior and lateral view to determine the position of the bone graft plug. Each bone was then evaluated with quantitative computer tomography (CT) scan (Model XCT 2000, Stratec Medizintechnik, Germany), as shown in Figure 5-9. Three scans of the graft were taken in the transverse plane of the bone in the middle of the graft site at 2 mm intervals, Figure 5-10. The bone mineral density value was determined for a 10 mm^2 area of graft in each scan, this area was selected by eye as the central area of the graft. The density values from the three scans were then averaged to give a bone mineral density for each graft plug.

Figure 5-9 - Scanning the graft in the CT scanner

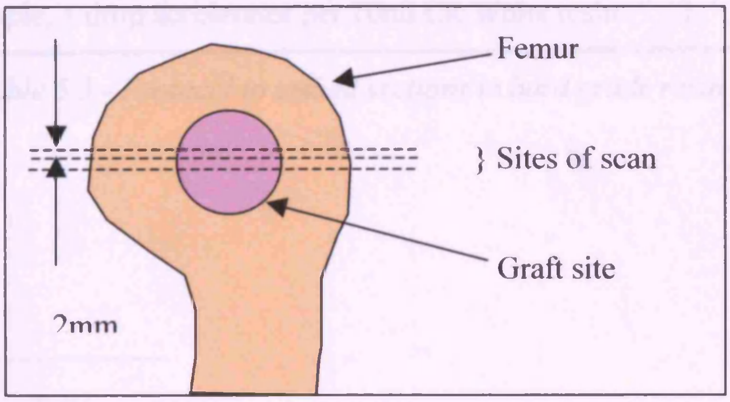

Figure 5-10 - Scan sites of the femur

5.2h Histology

To perform histology analysis, the samples were embedded in hard grade resin, from which micro sections could be cut and analysed. Initially the samples were fixed in formal saline[1], they were dehydrated using methylated spirit[1] and defatted using chloroform[1] and finally embedded and cast in LR white resin[2]. The steps are noted in Table 5.3. Once cast, the micro sections were cut using the Exakt Diamond edge cutting saw (Type 310CP)[3] using a 0.3mm thick blade. Technovit Glue[3] was used to stick the sections to a Perspex slide (~ 4 mm thick). The sections were ground using an Exakt micro grinding system[3] to a thickness of approximately 100μm and polished on the Motopol 2000[4] with polishing cloth and 0.5μm Alumina polishing solution[4]. Once prepared the sections were then stained with Tolidine Blue (20 minutes) and Paragon (25 minutes). To preserve the slides cover slips were placed over the section using Pertex mounting medium[5].

Step	No. of days
10 % Formal Saline (equivalent to 4% formaldehyde)	4
50% ethanol %50 distiled water under vacuum	2
100% ethanol (change after 2 days)	4
Chloroform (change after day two and three)	4
100% ethanol four days, change ethanol daily	4
50% LR White resin 50%ethanol under vacuum	2
100% LR White resin under vacuum (change after day four)	8
Cast sample, 1 drop accelerator per 10ml LR White resin	

Table 5.3 - Protocol to embed sections in hard grade resin

[1] BDH Laboratory supplies

[2] Agar Scientific Ltd

[3] Exact, Apparateban GMBH Robert-Koch-Strusse 5, D-22852 Nordestedt

[4] Buehler UK, Milburn Hill Rd, Coventry CV$ 7HS

[5] Merck

The slides were examined under a light microscope (10 x magnification) and images captured using a camera (JVC 3 CCD digital camera) mounted on the microscope. A line of 15 pictures was taken through each graft site from the left margin to the right. These pictures were taken 5 mm down from the top of the graft. Each image was imported into Adobe Photoshop 5.5 (Adobe Systems Incorporated, USA) and had dimensions of 14.5 cm x 10.5 cm. A grid with a vertical and a horizontal line at 1 cm intervals was superimposed on the image. A note was then made of whether each intersect of the grid was covering, new bone, old bone or no bone. The percentage of each was determined by dividing each total by the total number of grid intersections (this is known as the line intersect method). The results from each picture was analysed to show variations in bone incorporation across the graft site. The results from the 15 pictures were also averaged to give values for each specimen.

In addition to histology of the in-vivo samples, at least five impacted samples from each group in the mechanical study were also set in hard grade resin and sectioned for analysis. The protocol for the mechanical samples was similar to the in-vivo samples. However, all the bone was categorised as old bone, and only eight pictures were taken and averaged per sample. The percentage of area containing no bone was categorised as the porosity of each sample.

5.3 Results

Five samples were tested mechanically for each group. In the in-vivo study three of the tibial defects were created too low, where there was very little cancellous bone. Consequently the graft was not constrained and fell into the tibia medullary canal. These cases were omitted from the statistics results. The remaining sample numbers are displayed in Table 5.4.

	Graded	Small	Large
Six weeks	n = 5 (1×T, 4×F)	n = 5 (3×T, 2×F)	n = 5 (2×T, 3×F)
Twelve weeks	n = 5 (2×T, 3×F)	n = 4 (2×T, 2×F)	n = 4 (1×T, 3×F)

Table 5.4 - Sample numbers in each group, where T is the number of samples in the Tibia and F is the number in the femur.

The results were taken as non-parametric data since the sample groups were small. Statistical analysis was conducted using the Mann Whitney U test for independent samples and the Wilcoxon test for related samples. The significance was set as $p \leq 0.05$.

5.3a Compaction of the graft samples

The height of each five gram sample prior to impaction varied between specimens; Small (34.3 mm ± 2.16) Large (40.1 ± 3.47) and Graded (34.8 mm ± 1.30). The Large graft samples were significantly higher than the other groups ($p = 0.004$). To normalise the data the start height was deducted from the height measurements. The average impaction curves for the Graded, Small and Large groups is illustrated in Figure 5.10. The large graft showed the greatest compaction after 100 impacts, although this was not significant (Figure 5.11). However the Graded showed significantly more impaction during the first seven impacts than the Small graft (p = 0.01, 0.016, 0.02, 0.025, 0.037, 0.045 and 0.037).

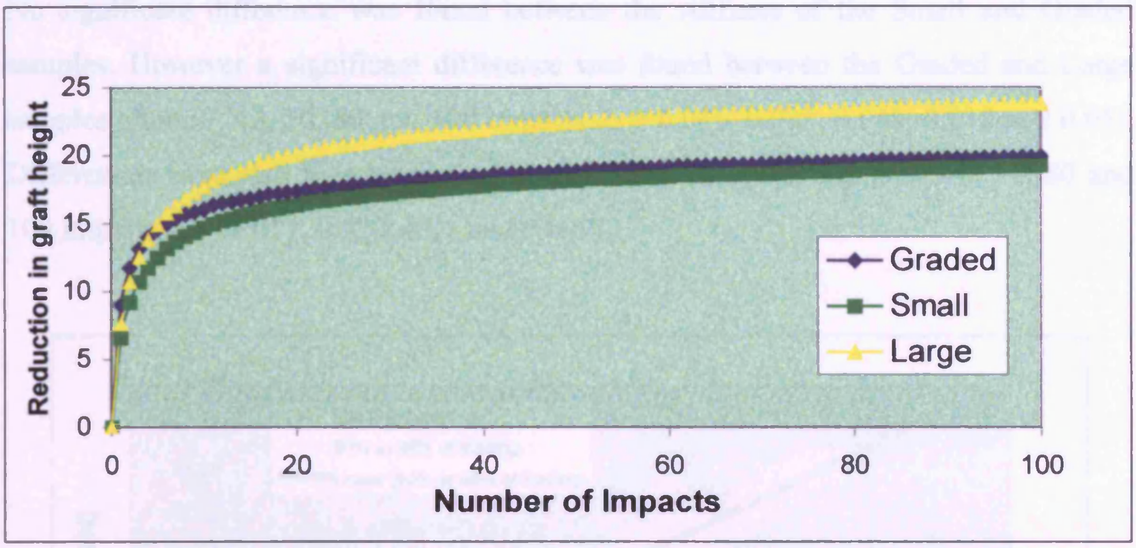

Figure 5.10 - Average reduction in height of graft in cylinders during 100 impactions

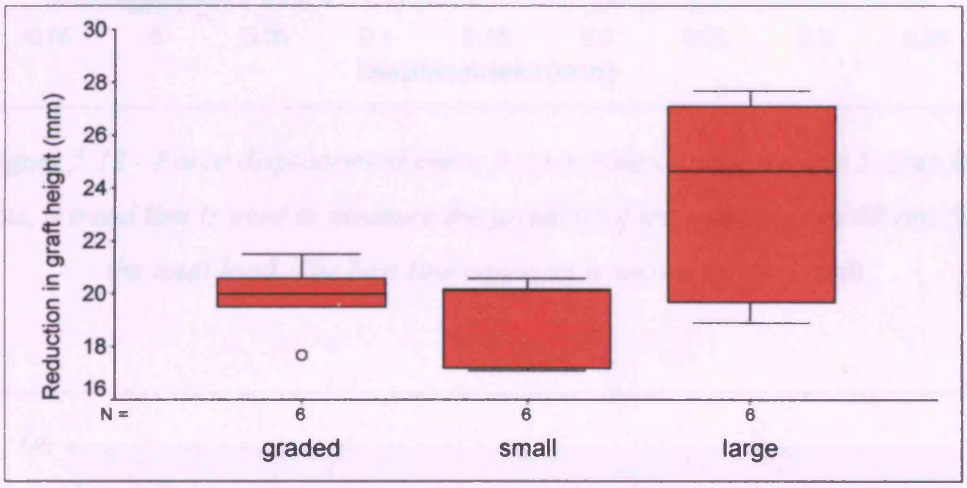

Figure 5.11 - Total reduction in sample height after a hundred impacts

5.3b Mechanical stiffness of the impacted samples

To determine the compressive modulus of a sample, a straight line was placed on the force displacement graph between 60 to 98% of the final load (Figure 5.12), and the gradient of the straight line equation taken as the force divided by extension. The stiffness' for all graft types are displayed in Figure 5.13. The average stiffness (± standard deviation) after 100 impacts was: Graded 104.7 MPa ± 23.5, Small 115.5 MPa ± 22.7 and Large 70.6 MPa ± 9.1, which is illustrated as a box plot in Figure 5.14.

No significant difference was found between the stiffness of the Small and Graded samples. However a significant difference was found between the Graded and Large samples after 30, 40, 50, 80 and 100 impacts ($p = 0.045, 0.028, 0.045, 0.018$ and 0.05). Differences were also found between the Small and Large group after 40, 50, 80 and 100 impacts ($p = 0.017, 0.028, 0.01$ and 0.009).

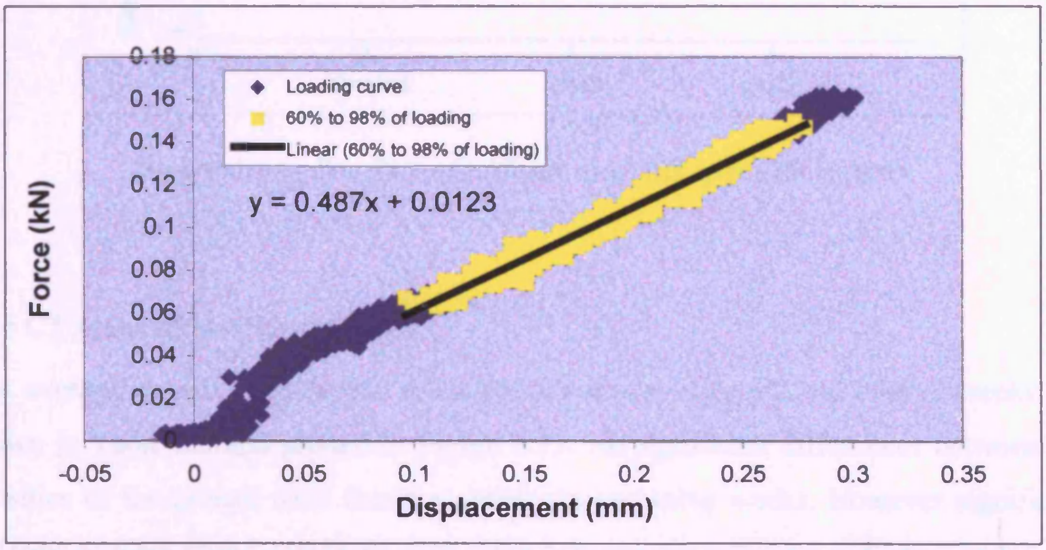

Figure 5.12 - Force displacement curve from testing Graded sample 5 after five impacts, a tread line is used to measure the gradient of the line between 60 and 98% of the total load. The best line equation is shown on the graph

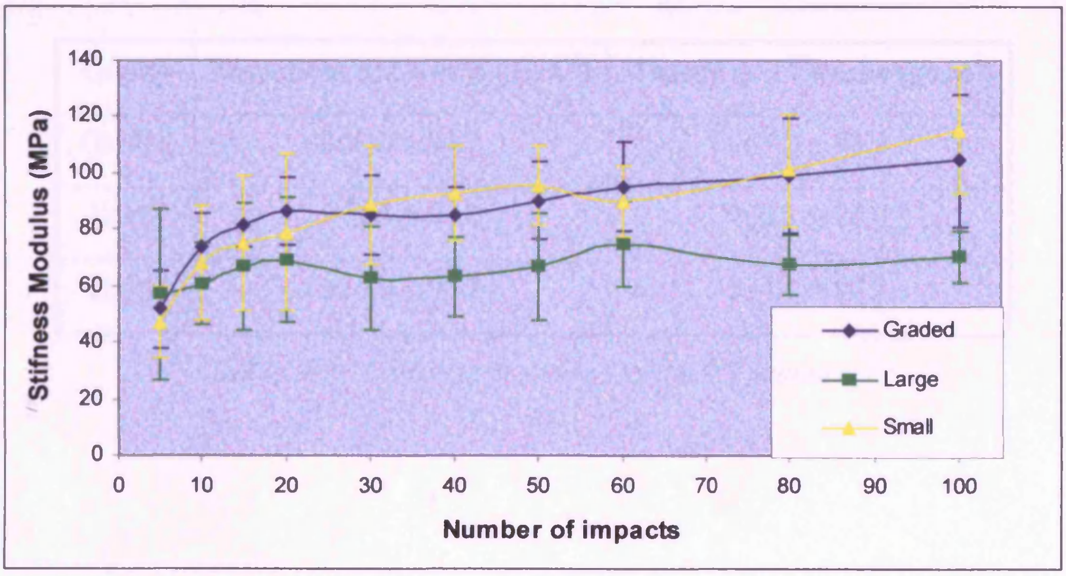

Figure 5.13 - Stiffness modulus for the Graded, Large and Small graft samples, error bars show standard deviation

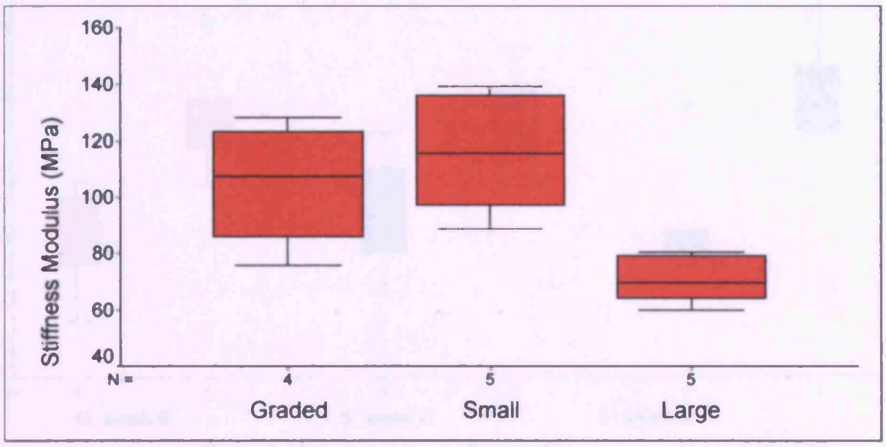

Figure 5.14 - Box Plot of stiffness modulus after 100 impacts

5.3c CT scans of In-vivo samples

The average densities, measured from the CT scans, after six and twelve weeks are shown in Table 5.5 and plotted in Figure 5.15. No significant differences between the densities of the groups were found at either six or twelve weeks. However significant differences were found within all graft types between the two time periods (Graded p = 0.016, Small p= 0.047, Large p = 0.047). Figure 5.16 shows an example of the pictures produced from the CT scans. Figure 5.17 is a CT scan of the empty sites left for twelve weeks in a tibia and femur. Unfortunately the defect was created too low in the tibia and there is little surrounding cancellous host bone.

Group	Density at Six weeks (g/cm^3)	Density at 12 weeks (g/cm^3)
Graded	308.0 ± 84.2	469.2 ± 88.5
Small	329.3 ± 91.9	460.3 ± 78.4
Large	326.9 ± 90.1	514.5 ± 87.7

Table 5.5 - Densities measured by the CT scanner

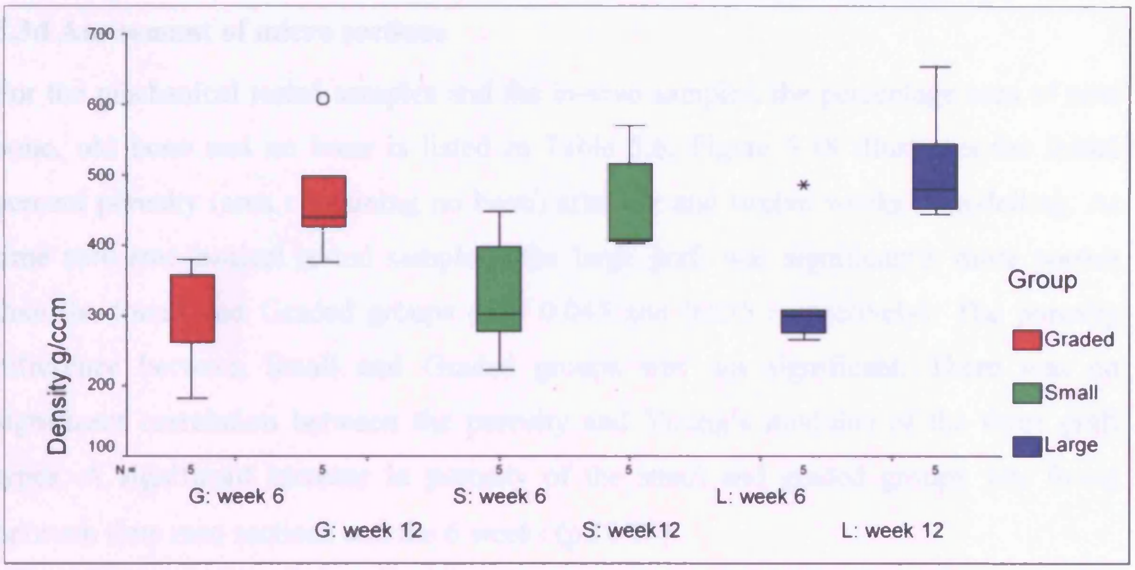

Figure 5-16 - Box plot of density measurements from the CT scanner

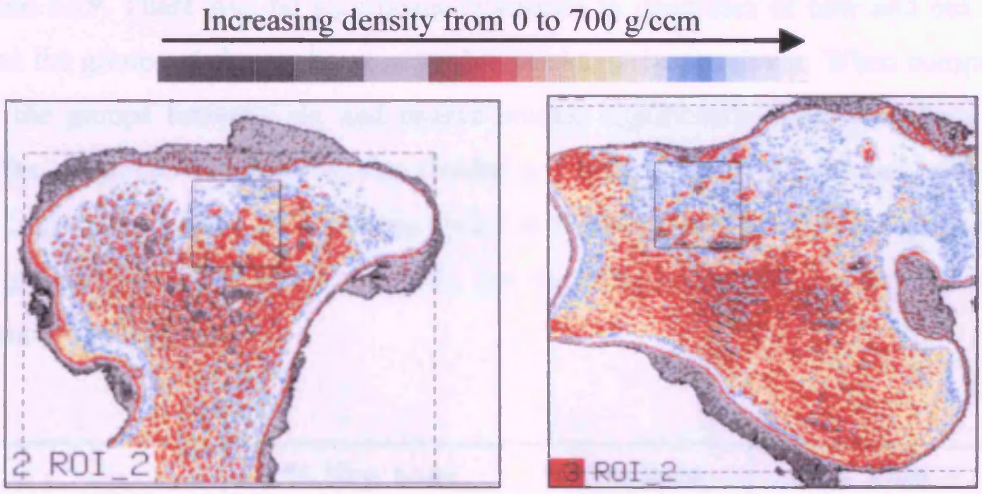

Figure 5-17 - Example of CT scan pictures of Large graft after 12 weeks in a tibia (left) and femur (right)

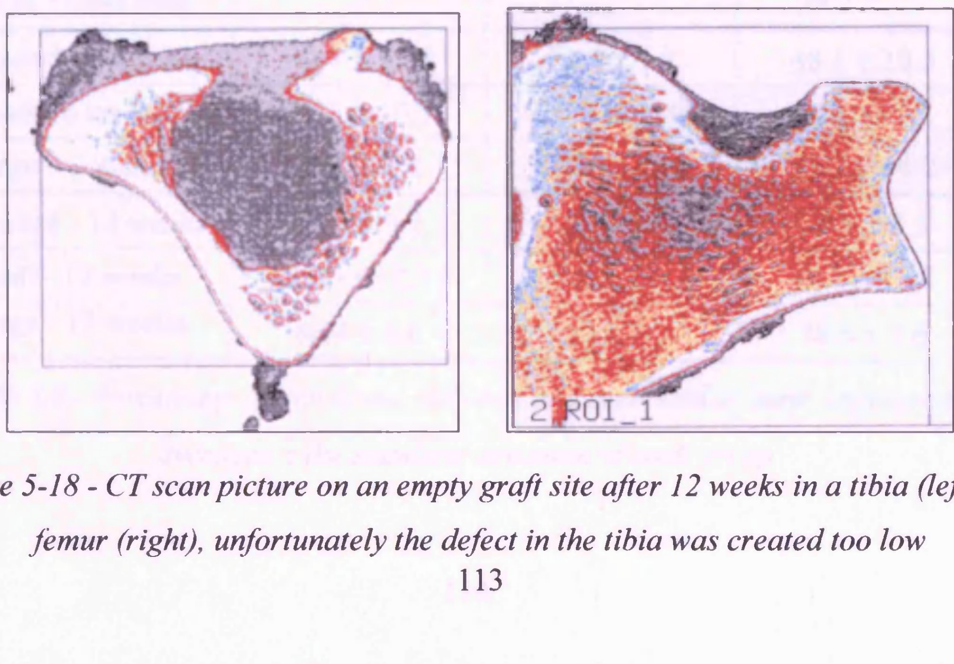

Figure 5-18 - CT scan picture on an empty graft site after 12 weeks in a tibia (left) and femur (right), unfortunately the defect in the tibia was created too low

5.3d Assessment of micro sections

For the mechanical tested samples and the in-vivo samples, the percentage area of new bone, old bone and no bone is listed in Table 5.6. Figure 5.18 illustrates the initial percent porosity (area containing no bone) after six and twelve weeks remodelling. At time zero (mechanical tested samples), the large graft was significantly more porous than the Small and Graded groups ($p = 0.045$ and 0.035 respectively). The porosity difference between Small and Graded groups was not significant. There was no significant correlation between the porosity and Young's modulus of the three graft types. A significant increase in porosity of the small and graded groups was found between time zero sections and the 6 weeks ($p \leq 0.05$).

The percentage area of new and old bone for the samples in the in-vivo study is plotted in Figure 5.19. There was no significant difference in quantities of new and old bone between the groups at six weeks or at twelve weeks post-operatively. When comparing within the groups between six and twelve weeks, significantly more new bone was found for all groups at twelve weeks: Graded $p = 0.05$, Small $p = 0.05$ and Large $p = 0.014$. Significantly less old bone was found at twelve weeks in both the graded and Large groups ($p = 0.019$ and $p = 0.014$), but no differences were found between the areas unoccupied by bone.

	% New bone	**% Old Bone**	**% Void**
Graded - time zero	0	67.7 ± 3.9	32.3 ± 3.9
Small - time zero	0	68.8 ± 5.8	31.2 ± 5.8
Large - time zero	0	57.6 ± 7.9	42.4 ± 7.9
Graded - 6 weeks	40.7 ± 15.0	11.3 ± 9.8	48.1 ± 10.5
Small - 6 weeks	37.5 ± 10.5	10.9 ± 10.9	51.6 ±13.2
Large - 6 weeks	35.0 ± 8.2	11.6 ± 9.6	53.7 ± 14.2
Graded - 12 weeks	62.7 ± 9.2	2.0 ± 2.0	35.3 ± 8.5
Small - 12 weeks	55.0 ± 12.7	1.8 ± 1.6	43.7 ± 13.0
Large - 12 weeks	60.4 ± 6.6	1.0 ± 1.0	38.6 ± 7.6

Table 5.6 - Percentage of new bone, old bone and area void of bone, expressed as averages ± the standard deviation of each group

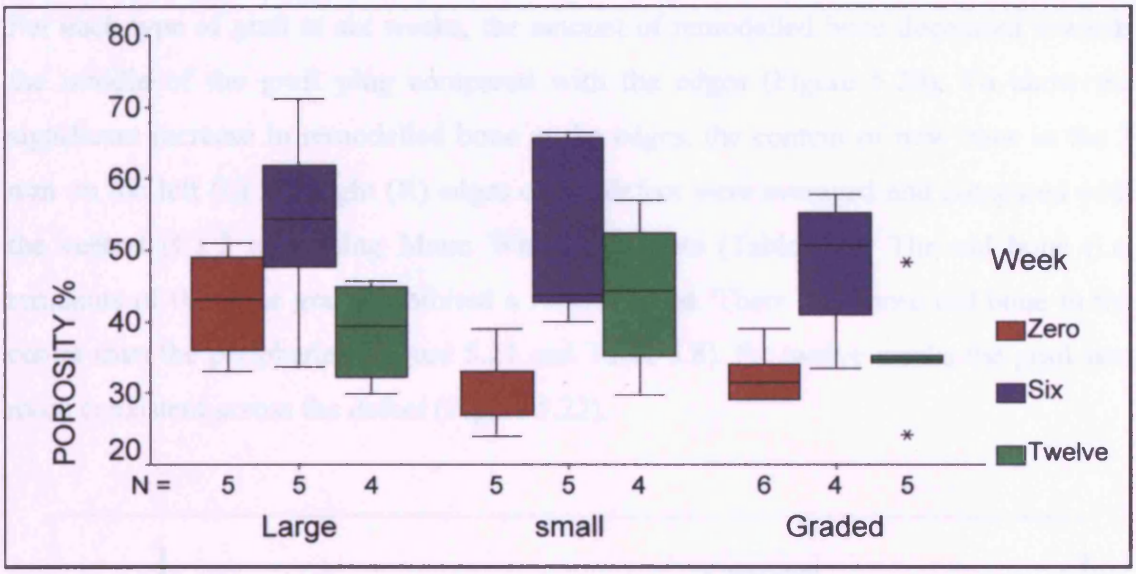

Figure 5.18 - Box plot of initial porosity of samples and after six and twelve weeks remodelling

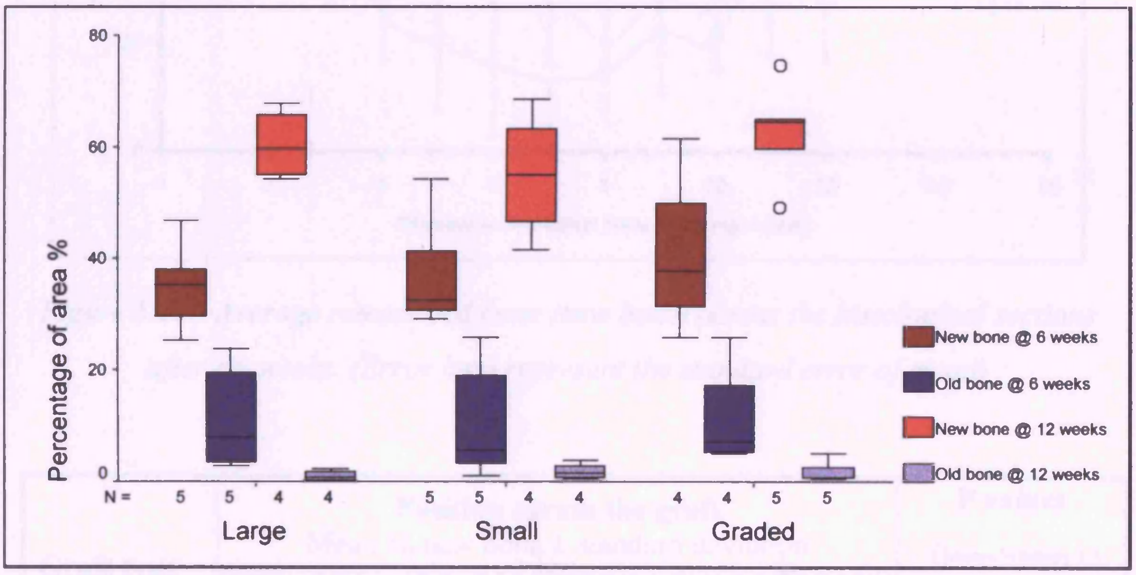

Figure 5.19 - Box plot of area containing new and old bone after six and twelve weeks in-vivo

For each type of graft at six weeks, the amount of remodelled bone decreased towards the middle of the graft plug compared with the edges (Figure 5.20). To show the significant increase in remodelled bone at the edges, the content of new bone in the 3 mm on the left (L) and right (R) edges of the defect were averaged and compared with the central (C) 3 mm using Mann Whitney U tests (Table 5.7). The old bone (i.e. remnants of the bone graft) exhibited a reverse trend. There was more old bone in the centre than the peripheries (Figure 5.21 and Table 5.8). By twelve weeks the graft was more consistent across the defect (Figure 5.22).

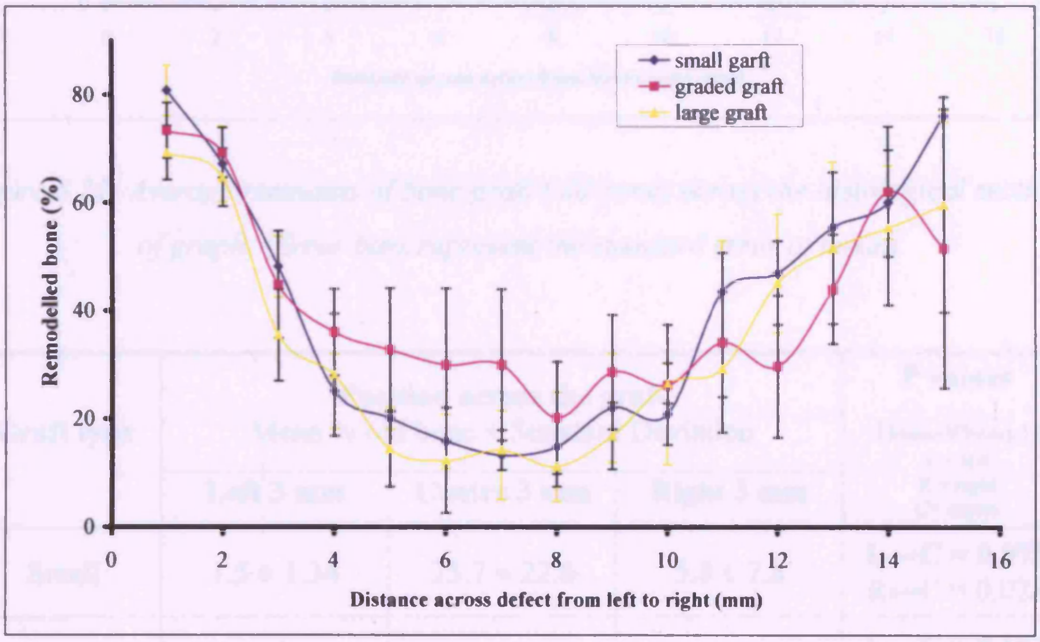

Figure 5.20 - Average remodelled bone (new bone) across the histological sections after six weeks. (Error bars represent the standard error of mean)

Graft type	Position across the graft Mean % new bone ± standard deviation			P values (Mann-Whitney U) L = left R = right C= centre
	Left 3 mm	**Centre 3 mm**	**Right 3mm**	
Small	65.4 ± 9.4	16.7 ± 17.0	63.0 ± 19.2	L↔C = 0.019 R↔C = 0.016
Large	56.5 ± 5.6	14.1 ± 7.8	70.8 ± 12.7	L↔C = 0.09 R↔C = 0.016
Graded	62.5 ± 12.0	26.7 ± 22.4	54.9 ± 21.8	L↔C = 0.021 R↔C = 0.083

Table 5.7 - Percentage of new (remodelled) bone across the bone graft plug at six weeks

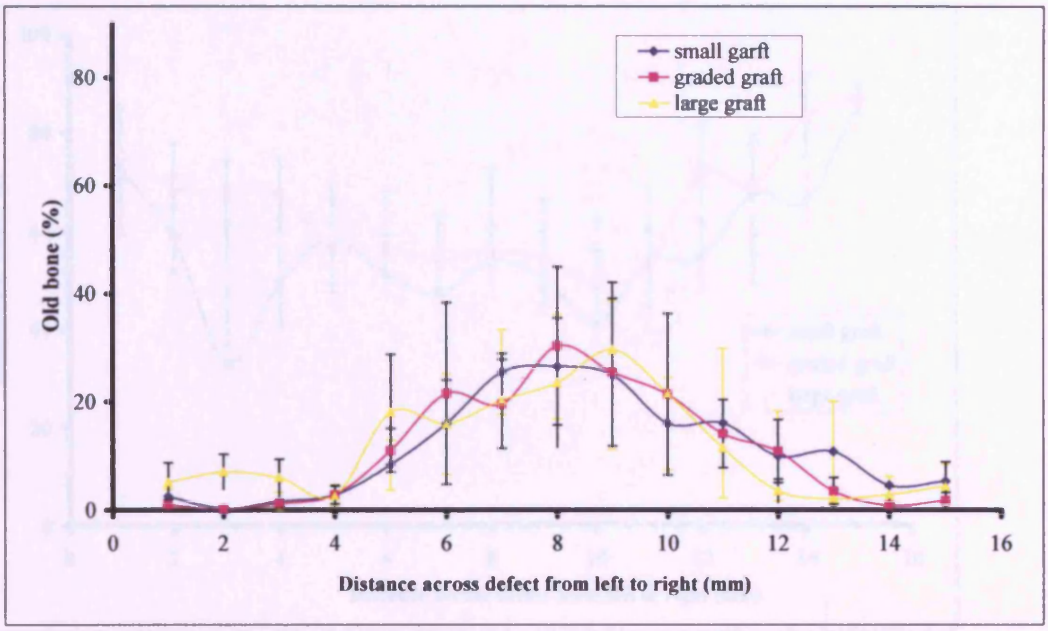

Figure 5.21- Average remnants of bone graft (old bone) across the histological sections of graph. (Error bars represent the standard error of mean)

Graft type	Position across the graft Mean % old bone ± Standard Deviation			P values (Mann-Whitney U) L = left R = right C= centre
	Left 3 mm	**Centre 3 mm**	**Right 3 mm**	
Small	1.5 ± 1.34	25.7 ± 22.6	5.8 ± 7.8	**L↔C = 0.075** R↔C = 0.028
Large	6.1 ± 6.7	24.5 ± 23.5	3.4 ± 3.6	**L↔C = 0.173** R↔C = 0.075
Graded	0.8 ± 0.8	25.2 ± 24.2	2.0 ± 2.0	L↔C = 0.021 R↔C = 0.043

Table 5.8 – Percentage of old bone graft across the defect at six weeks

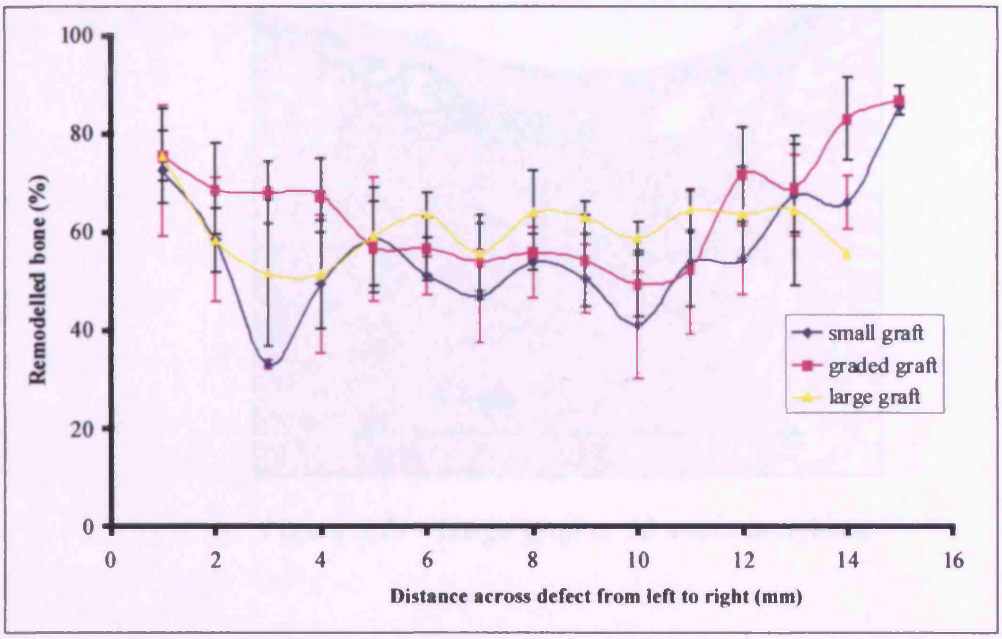

Figure 5.22 - Average remodelled bone (new bone) across the histological sections after twelve weeks. (Error bars represent the standard error of mean)

Examples of the three graft types impacted in the tufnol cylinders are shown in Figure 5.23. With the large graft it is possible to pick out the large pieces of graft, particularly cortical pieces. The small graft appears to have the most consistent appearance. The graded graft does not appear to have many medium sized pored other than those seen in a large chip of cancellous graft. Figure 5.24, Figure 5.25 and Figure 5.26 show the remodelled Large, Small and Graded graft after twelve weeks, by this stage there does not appear to be any obvious differences between them.

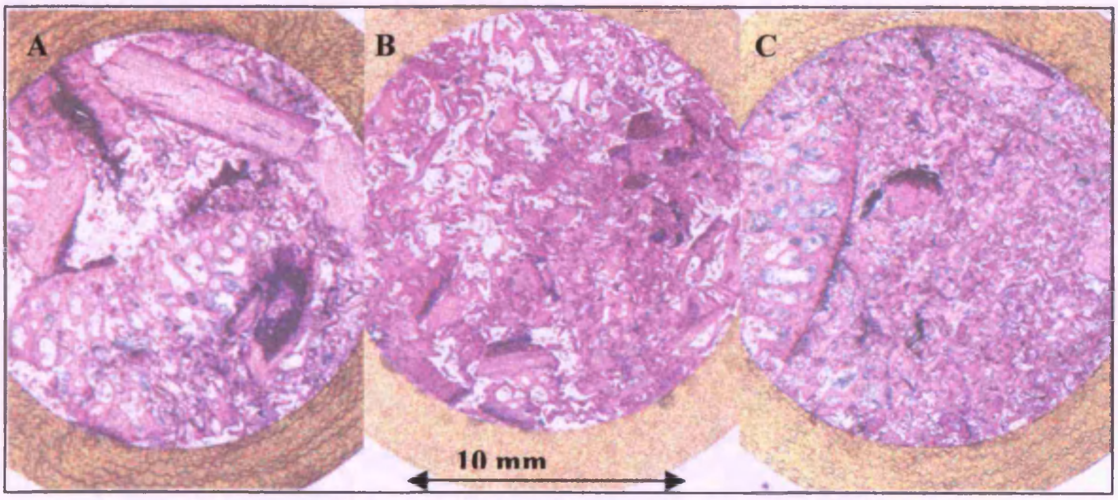

Figure 5.23 - Micro sections of graft after impaction in Tufnol® tubes, (A) Large, (B) Small and (C) Graded

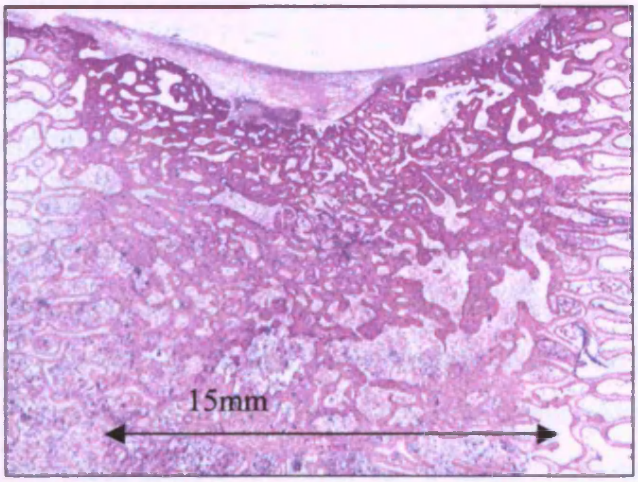

Figure 5.24 - Large graft at 12 weeks in a femur

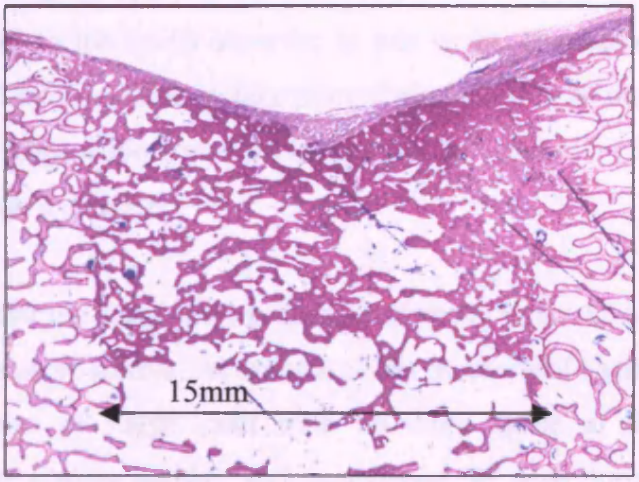

Figure 5.25 - Small graft at 12 weeks in a femur

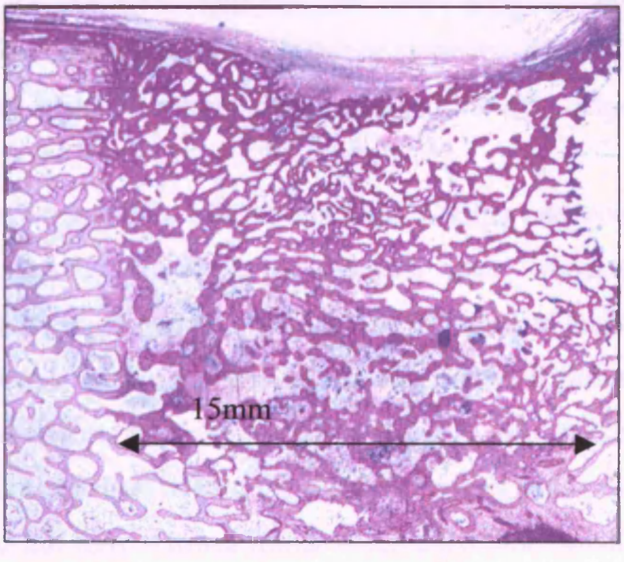

Figure 5.26 - Graded graft at 12 weeks in a femur

5.4 Discussion

The objective and aim of this part of my project was to determine the effect of different graft particles sizes on the mechanical and biological properties of impacted bone graft. Unfortunately clinical data of different surgeons impact forces measured during revision hip arthroplasty operations (Chapter 4) was not available when the impaction force of approximately 15 kN was chosen for this study. Impaction of bone graft into a 15 mm tube is similar to the distal impaction into a revision femur (Stryker Howmedica's revision bone plug size range is 10 to 16 mm). The average forces calibrated as passing through the impactor during distal impaction were 2.8 to 7.6 kN (Chapter 4), which implies that the force chosen was at least double what the graft would experience during impaction grafting surgery. It is therefore unlikely that in a revision situation the graft would be compacted to the levels observed in this study. The majority of compaction and increase in stiffness appeared to take place during the first twenty to thirty impacts. Therefore with the impact force used in this part of the study (~ 15 kN), one hundred impacts was probably excessive.

The results found that the Large graft behaved differently to the Small and Graded graft groups, which were more similar. At the start of the mechanical testing it was noted that the 5 gram samples of Large graft took up more space in the Tufnol® tubes (significantly higher starting height), and compressed the most during the 100 impacts (not significant). It is not surprising that the Large graft consumed a larger volume initially, as one would expect the uncrushed samples to have larger voids due to the natural packing of the particles. Although the Large graft appeared to compress the most, it still had significantly higher percentage porosity (42.2 %) after 100 impacts than the other groups, which may have contributed to its lower compressive stiffness.

The Small and Graded samples had similar start heights and compressed to similar amount after 100 impacts. However for the first seven impacts the Graded graft compacted significantly more than the Small graft. The Graded graft is designed to have the smallest void spaces, as the intention of the distribution is that the smaller particles fill the void spaces between the large particles, however it is unlikely that the particles will naturally position themselves into the ideal formation. This probably explains why the Graded graft did not have a lower initial volume than the Small. Also it is possible that the large graft particles in the Graded samples created bulky initial voids which collapsed under compaction, hence the variation in the first seven impacts.

The micro sections showed an initial increase in porosity by six weeks (significant only in the small and graded groups), followed by a decrease in porosity (non significant). However the CT analysis did find that the densities of the samples were increased significantly between six and twelve weeks for all three groups. This anomaly might be due to the new bone having a higher mineral density than the decaying old bone. The CT data did not find any differences between the groups at six or twelve weeks, which corresponds with the porosity findings.

The histology of all graft groups showed an increase in new bone from six to twelve weeks, and only minor remnants of the original allograft by twelve weeks. Analysis of the six week histology sections found significantly more new bone at the edges of the cylinder for all graft types. This was no-longer the case by twelve weeks. This demonstrates that that all the graft types displayed osteoconductive properties, hence the gradual remodelling of the graft from the peripheries. Such complete remodelling of the graft by twelve weeks would not be expected in a revision arthroplasty situation where the vascular supply may be limited and the natural bone turnover reduced.

The mechanical testing was performed in the Dartec loading machine using a load cell of 50 kN, but the tests performed were under 200 N, which is only 0.4 % of the load cells range. Therefore the errors in the testing would have been large, which may have been a contributing factor to the large deviations seen in the mechanical stiffness results. Ideally a loading machine with a smaller load cell should have been used.

The graft in the mechanical aspect of this study was not irradiated, unlike that used in the in-vivo part of the project. Irradiating graft is known to have an effect on the mechanical properties of bone (Stevenson, 1999), so it is possible that the stiffness and therefore the measured confined stiffness moduli of the samples may have been lower if the graft had been irradiated. If the graft particles had been weaker because of irradiation it is possible that they were more compacted, but this would only be a very minor difference.

The model used was very similar to that described by Griffon et al (2001). Unfortunately it was hard to repeatedly drill a hole for the graft high enough in the tibia to ensure it was in cancellous bone, and not the medullary canal. Also cancellous bone in distal femur is much denser than that in the proximal tibia. For these reasons the recommendation for any future studies is to only use the distal femoral graft site.

The small and graded group behave very similarly in this model implying that the complicated grading is unnecessary. Unlike other studies the large graft was inferior mechanically. However the test was axial and did not measure the shear strength required to support an implant.

5.5 Conclusion

The increase in porosity of the Large group compared with the Small and Graded groups did not appear to affect the remodelling rate. However the Large graft did appear inferior in axial mechanical testing. The complicated grading of particle size did not show any significant advantages on the remodelling or axial stiffness. The use of small graft between 2 to 4 mm is therefore recommended from these findings.

In the Small and Graded groups the percentage porosity increased significantly between time zero and six weeks. For all graft groups the bone mineral density was significantly higher at twelve weeks compared to six weeks. The density of bone can be directly related to mechanical strength (Augat, et al 1998), which implies that during the early stages of remodelling the graft resorbs and mechanical stiffness decreases. However by twelve weeks more new bone is laid down and the mechanical stiffness increases.

Chapter 6

Mechanical Strength and Histology of BoneSave™ in an Ovine study

6.1 Introduction

BoneSave™ (Stryker® Howmedica Osteonics Inc, Allendale, NJ, USA) is a composition of 80 % Tricalcium Phosphate and 20 % Hydroxyapatite, which comes in a granular form. It has been developed as a bone graft extender, with particular emphasis on its use in impaction grafting of revision hip replacements. It has been the subject of several mechanical and in-vivo studies as discussed in the Literature Review (Section **2.5**). Clinical trials of impaction grafting in the acetabulum using 50:50 mix of BoneSave™ and allograft are currently underway.

In the previous chapter a study into the affect of allograft size on remodelling was investigated in an ovine model. The results found that the graft size did not have any effect on the remodelling rate, however a reduction in the density of the impacted allograft after six weeks was discovered, which recovered by twelve weeks. Previous work by Augat et al (1998) has shown that the density of bone can be related to the mechanical strength. It is therefore possible that this reduction in density during remodelling of the graft may also correspond with a reduced mechanical strength. A probable cause of the low density is osteoclastic bone resorption prior to vascular ingrowth and the formation of new bone by osteoblasts. An ovine study (Pratt, 2002) has indicated that BoneSave™ takes a long time to be resorbed and replaced with bone as compared with allograft. **It is possible that the inclusion of BoneSave™ could slow down resorption and hence maintain the mechanical strength of the graft during remodelling. It is hypothesised that the mechanical strength of remodelling allograft is lower at six weeks than twelve weeks after implantation, and that addition of an equal quantity of BoneSave™ to allograft will produce higher mechanical stiffness six weeks post-operatively than allograft.**

To test this theory an ovine in-vivo study was conducted comparing a 50:50 mixture (by mass) of BoneSave™ and allograft, with allograft. The study was similar to that conduced in Chapter 5, with six sheep allocated to six weeks and a further six to twelve weeks. However the study in Chapter 5 had found a marked difference in the remodelling in the defect of the distal femur compared with the proximal tibia, and also highlighted a tendency to create the defect too low in the tibia, thereby missing the cancellous bone. Hence a 15 mm defect in the medial femoral condyles of both legs was chosen as paired test sites. To compare the mechanical properties of the different groups, compressive modulus of the retrieved samples was derived by non-destructive mechanical testing. Non-destructive testing was chosen to enable histology analysis to also be carried out.

The 50 % porous BoneSave^{TM} granules have a pore size of 400 – 600 μm and an interconnectivity pore size < 100 μm. It is available in 40 grams sterile packets of two size ranges, 2-4 mm and 4-6 mm, only the 2-4 mm size was used for this project.

6.2 Methodology

Twelve sheep were used in this study; each received a 15 mm diameter cylindrical defect, approximately 15 mm deep, in the distal femur of both hind legs. One defect was filled with a 50:50 mix of BoneSave™ and allograft (Group B), the other with pure allograft (Group A). Half were terminated at six weeks and half at 12 weeks. After euthanasia the specimens were analysed by CT scans, non-destructive mechanical testing and micro section histology.

6.2a Graft preparation

The graft was prepared in a similar fashion to that used in Chapter 5 (Section **5.2a**). Sheep femurs and tibias were collected from an abattoir the day after slaughter, all soft tissue and cartilage was resected from bones. The allograft was milled in the Lere Bone mill[1] and washed following the North London Tissue Bank Protocol, as detailed in Table 5.1 (Figure 6.1 A&B). The graft was not sieved, but any big pieces (over 10mm) were removed by hand. A 40 gram packet of 2 - 4 mm BoneSave™ was combined with an equal mass of the prepared allograft and thoroughly mixed. In the graft sized study (Chapter 5), 15 mm diameter Tufnol® cylinders were used to contain the graft. However for this project Acetal[2] tubes were used due to cost and ease of machining (Acetal has an Elastic modulus of 3.3 Gpa). Twelve tubes were filled with 3.5 grams of the mixed substance, a further 12 tubes were filled with 3.5 grams of allograft. Once filled, caps were placed on each end of the tubes and secured into place with tape to prevent the graft escaping. The filled tubes were then double packed (Figure 6.1 C), frozen, and irradiated between 30 and 35 KGrays whist stored on dry ice to prevent thawing. The samples were removed from the freezer a couple of hours prior to surgery, to defrost at room temperature.

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[1] DePuy International, St. Anthony's Road, Leeds, LS11 8DT

[2] Acetal, Delrin

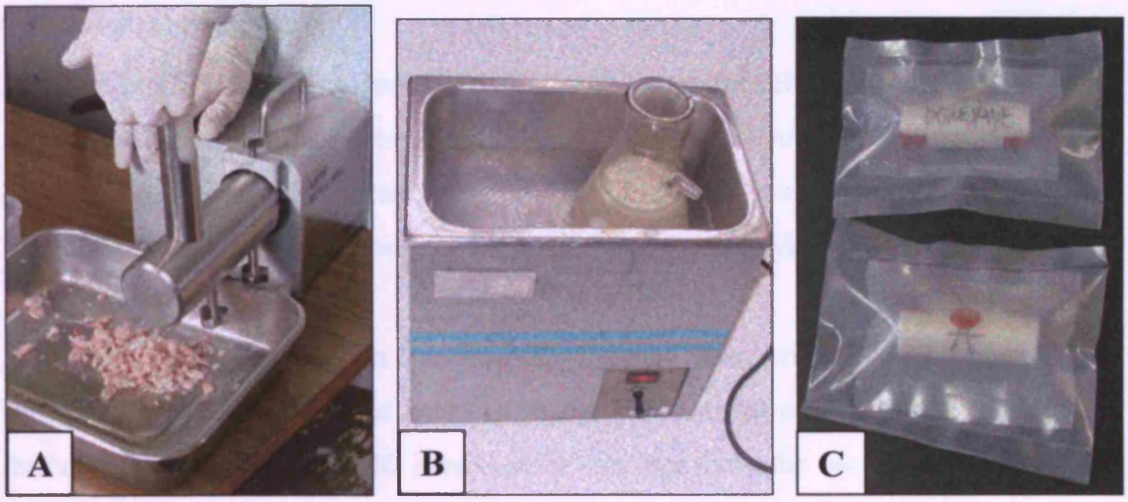

Figure 6.1 - Graft preparation: (A) morsellising, (B) washing and (C) packing

6.2b Impacting the graft

Whilst the surgery was being performed the graft was impacted in the autoclavable impaction jig, described in Section **5.2d**. In the graft size study (Chapter 5) the allograft was impacted in the jig using a drop height of 200 mm for the sliding mass, which produced a force of approximately 15 kN. However the results from force measurements in surgery (Chapter 4) were not available at the time, but these later proved that 15 kN was greater than the graft was likely to receive in surgery. The intra-operative measurements found that the average force in the distal impactor ranges between 2.8 and 7.6 kN (Chapter 4). A force of approximately 4kN, created by a drop height of 30 mm, was chosen for this study because it lay within the measured surgical range. Also trials in the lab showed that this force did not crush the BoneSave™ excessively. The number of impacts remained as 100. Figure 6.2 shows an impacted BoneSave™/allograft sample in an acetal tube.

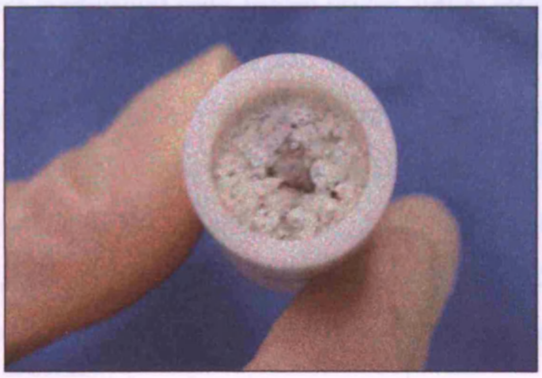

Figure 6.2 - Impacted BoneSave™/Allograft sample in tube

6.2c Surgical Procedure

All the surgical procedures (including the pre and post operative care) conformed to the Animals (Scientific Procedures) Act 1986 and were carried out by Professor Blunn with an anaesthetist, while I impacted the graft in the jig. The test site was a 15 mm diameter hole, approximately 15 mm deep, in the medial femoral condyle.

Both femurs were operated on consecutively for each sheep with allocation of graft type to left and right leg alternated between sheep. The surgical procedure was identical to that described in Section **5.2f.** However in this case only the two femoral sites were used and not the tibial sites. Postoperatively the sheep were individually penned for at least two weeks, and thereafter group housed. After euthanasia the distal femurs were removed and all soft tissue cut of from the bone.

6.2d Computer Tomography Scans

Three CT scans were taken at the centre of each test piece at two millimetre intervals using machine Model XCT 2000 (Stratec Medizintechnik, Germany). Densities were measured from a ten millimetre square in the middle of the test site for all three scans. These were then averaged to give a density figure for that sample.

6.2e Mechanical Testing

In order to preserve the specimens for histology, non-destructive mechanical testing was chosen. During the graft sized project (Chapter 5) mechanical analysis was executed on samples impacted in the lab (not for the in-vivo study). Unfortunately the results were inconsistent. In that study the Dartec loading machine performed the tests, which consisted of loading to 0.3 mm at a rate of 0. 5mm/second. The Dartec's load cell was 50 kN, but the tests were performed with forces under 500 N, outside the accurate range of the load cell. In addition the test did not take into account the visco elastic properties of the bone. Consequently the mechanical tests of the BoneSave™ study were performed in a Zwick materials testing machine (BDO-FB0.5TS)[1] with a 500 N load cell with accuracy within 0.2 % for the test range. To accommodate for the visco elastic properties of the bone, ten preconditioning cycles were included in the test. Although most published studies have used displacement control to test their samples (Linde and

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[1] Zwick

Hvid, 1989; Augat et al, 1998; Orr et al, 2001; Giesen et al, 1999; Yano et al, 2000), some publications also described resetting the strain channel after each loading cycle to accommodate the visco elastic creep (Linde and Hvid, 1989; Augat et al, 1998). However this was not possible with the Zwick. With this knowledge, and the problems encountered during the mechanical testing of the Graft-Sized project, a compressive force-controlled test was used.

To prepare the defects for testing 16 mm discs were cut from each sample in the Exact diamond edge cutting saw using a specially designed jig to ensure the cut was perpendicular to the long bone (Figure 6.3). The disc cut through the cylindrical test site at 4 mm from its proximal end, exposing a graft area of approximately 15 × 13 mm.

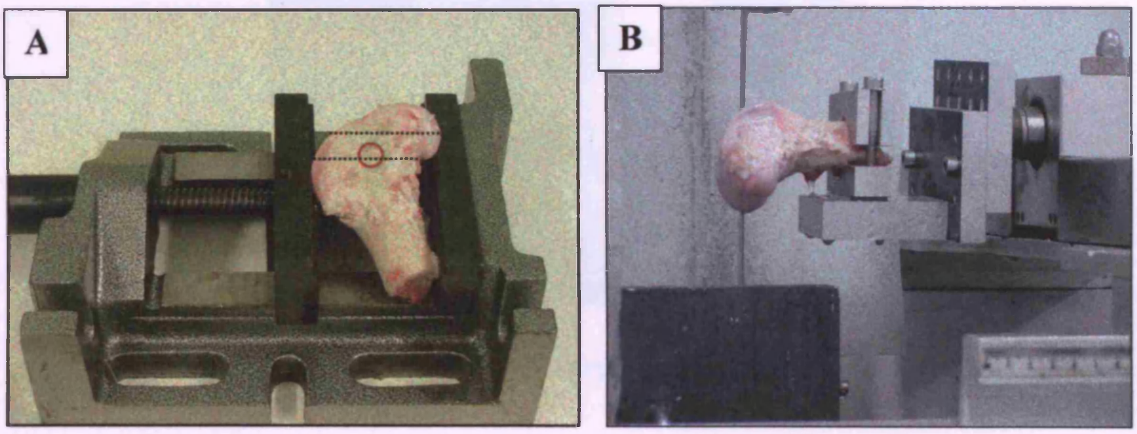

Figure 6.3 - (A) Position of disk, (B) Cutting a disk on the Exact saw

A 10 mm square head impactor was used for the mechanical tests, the centre of the exposed graft area was used as the test site and a second area on the lateral side of the femur was also tested to act as a control. The test was made up of several parts, initially the impactor was brought into contact with the bone to a force of 20 N, then 10 preconditioning cycles were applied to the bone (20 – 80 N) and finally the load was ramped to 400 N. The entire test was performed at 2 mm/min. The samples were tested in saline to prevent dehydration.

The compressive modulus was calculated from the gradient of the force displacement graph using the method described in Section **5.2e**. Again the resulting compressive modulus cannot be described as the Young's modulus of the sample because it is confined within the rest of the cancellous bone. Also the sample was mounted on the cross section of the bone, as apposed to an area matching the cross section of the impactor.

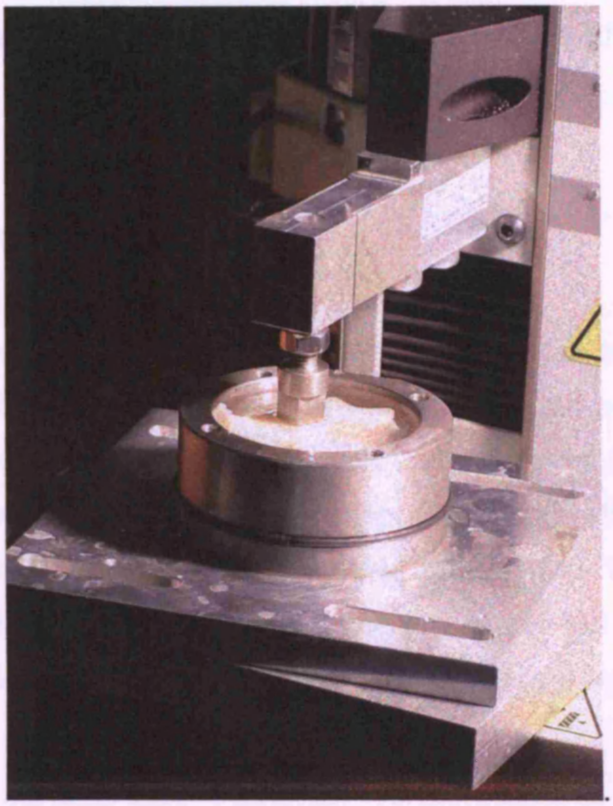

Figure 6.4 - Mechanical testing of a sample in the Zwick

6.2f Histology

Once the mechanical testing had been performed the samples were fixed in formal saline, embedded in LR white hard grade resin and micro sections cut from the centre of the defect as described in Section **5.2h**. Micro sections were made from one impacted sample of each graft type to give a time zero comparison. The sections were examined under light microscope and pictures taken using a digital camera (JVC 3 CCD) mounted on to the microscope. Pictures were also taken of each defect, whilst the slides were sitting on a light box with the camera mounted on a zoom lense. To determine the quantities of bone and BoneSave™ in these pictures a 7.5 mm grid was placed over the centre of the sample area. The percentage of bone and BoneSave™ was calculated as the number of intersects covering bone, or BoneSave™ divided by the total number of intersections in the grid.

6.3 Results

For comparison between the groups at the same time period, Wilcox paired tests were used. In all other cases Mann Witney U tests were used. The significance level was set at $p \leq 0.05$.

6.3a Computer Tomography Scans

CT scanning showed a significant higher density's of the samples in Group B compared with Group A, at both 6 and 12 weeks (Wilcoxon Paired test p = 0.28, p = 0.28). However, there was no statistical difference in the density of the allograft groups between 6 and 12 weeks, or the BoneSave™ group. Figure 6.5 is a box plot of density at six and 12 weeks. Results from the Graft-Size project have been included as a comparison. Figure 6.6 illustrates scans of Group A at six and twelve weeks post implantation, and Figure 6.7 Group B. The white region is that of highest density.

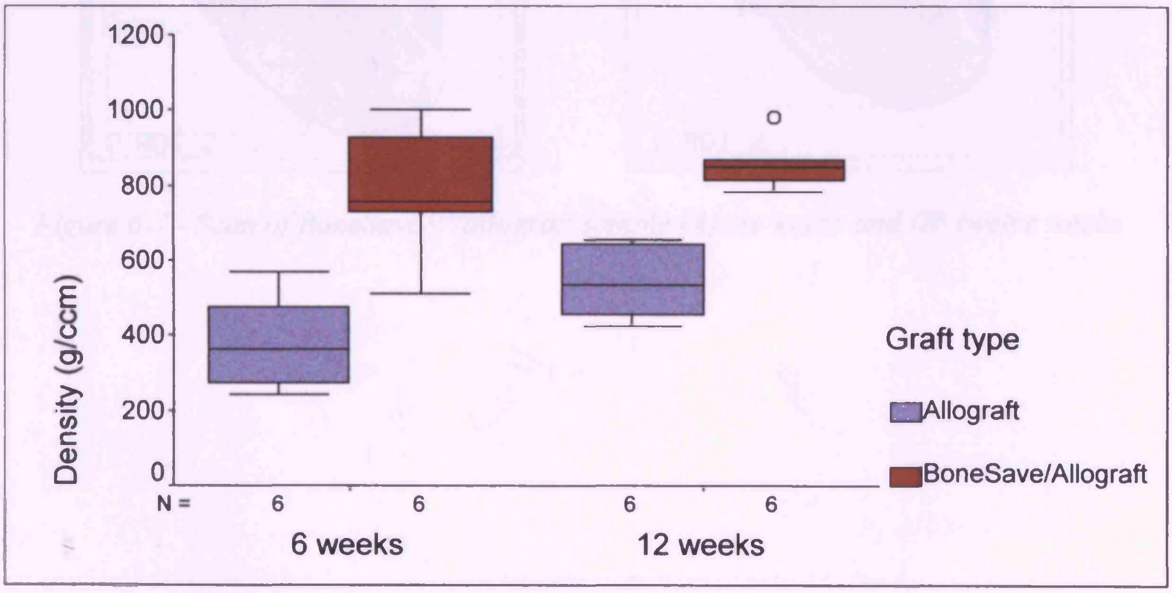

Figure 6.5 - Box plot of densities at six and twelve weeks

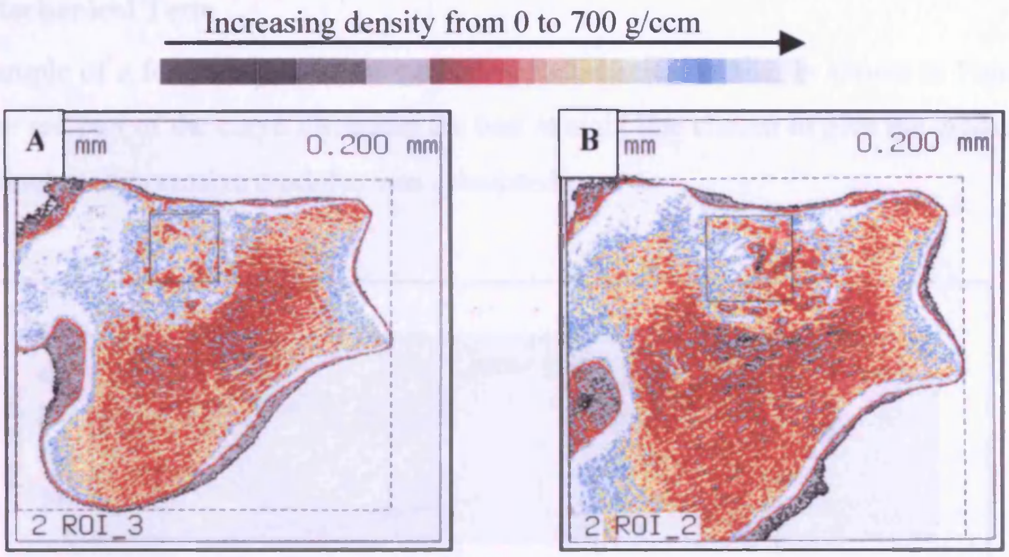

Figure 6-6 - CT scans of allograft group at (A) six weeks and (B) twelve weeks

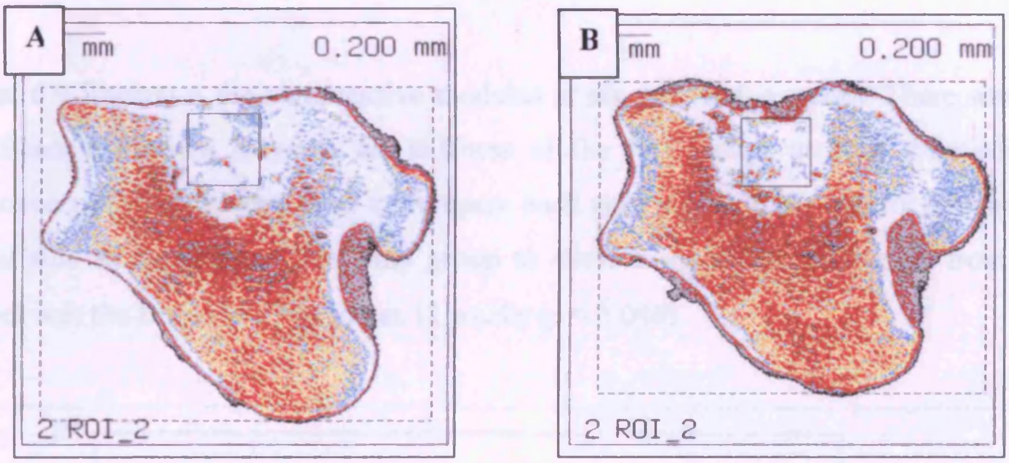

Figure 6-7 - Scan of BoneSave™/allograft sample (A) six weeks and (B) twelve weeks

6.3b Mechanical Tests

An example of a force displacement curve from mechanical testing is shown in Figure 6.8. The red part of the curve illustrates the best straight line chosen to give the gradient from which a compressive modulus was calculated.

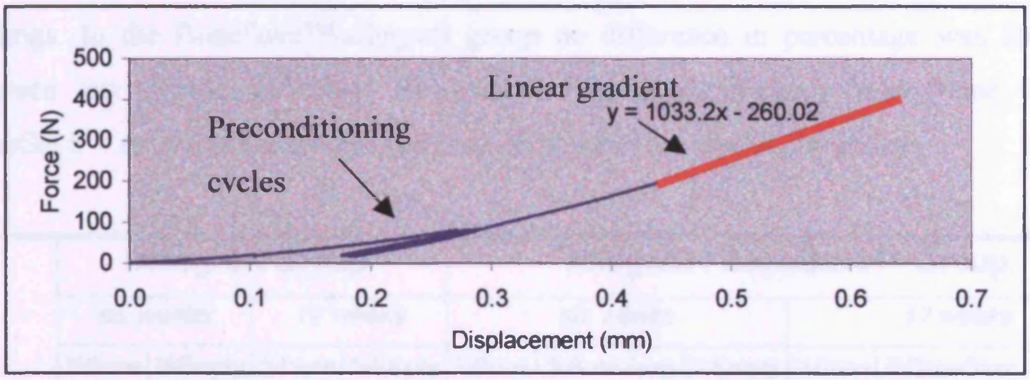

Figure 6.8 - Force displacement curve of mechanical testing

Figure 6.9 illustrates the compressive modulus at six and twelve weeks. There was no significant difference between the stiffness of the two groups at both time points. Wilcoxon paired tests were used to compare each graft site with the control site on the lateral side of the femur. The only group to show a significant difference from the control was the BoneSave™ group at 12 weeks ($p = 0.046$).

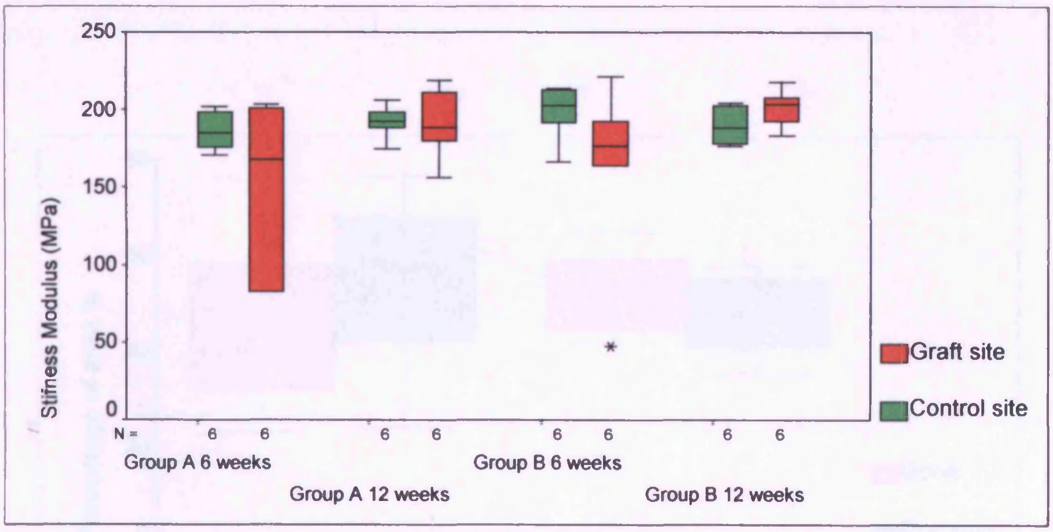

Figure 6.9 - Box plot of compressive modulus

6.3c Histology

The histology found that in some cases a layer of graft had fallen out of the top of the defect and in one case in the six week allograft group, most of the graft had fallen out. Table 6.1 gives the percentage of bone and BoneSave™ calculated from the histology pictures. In the Allograft group there was no significant difference in the volume of bone in the defect between six and twelve weeks, which correlates with the density findings. In the BoneSave™/allograft group no difference in percentage was found between any of the variables. However there was significantly more bone than BoneSave™ at twelve weeks ($p=0.05$), which was not the case at six weeks.

	Allograft Group				Allograft / BoneSave™ Group					
	six weeks		12 weeks		six weeks			12 weeks		
	%Bone	%Empty	%Bone	%Empty	%Bone	%BoneSave	%Empty	%Bone	%BoneSave	%Empty
	31.9	68.1	44.6	55.4	19.3	25.6	55.1	40	20	40
	23.1	76.9	53.7	46.3	38.9	35.8	25.3	29.1	29.1	41.8
	47.6	52.4	51.9	48.1	24.9	17.9	57.2	37.5	17.9	44.6
	76.1	23.9	59.3	40.7	35.8	38.6	25.6	40.7	26.6	32.7
	57.9	42.1	64.6	35.4	40.7	32.4	26.9	40	23.2	36.8
	31.9	68.1	42.1	57.9	36.1	24.6	39.3	41.1	23.2	35.7
Average	**44.8**	**55.3**	**52.7**	**47.3**	**32.6**	**29.2**	**38.2**	**38.1**	**23.3**	**38.6**
SD	**19.8**	**19.8**	**8.5**	**8.5**	**8.5**	**7.8**	**14.8**	**4.6**	**4.1**	**4.4**

Table 6.1 - Percentage of Bone and BoneSave™ calculated from histology pictures

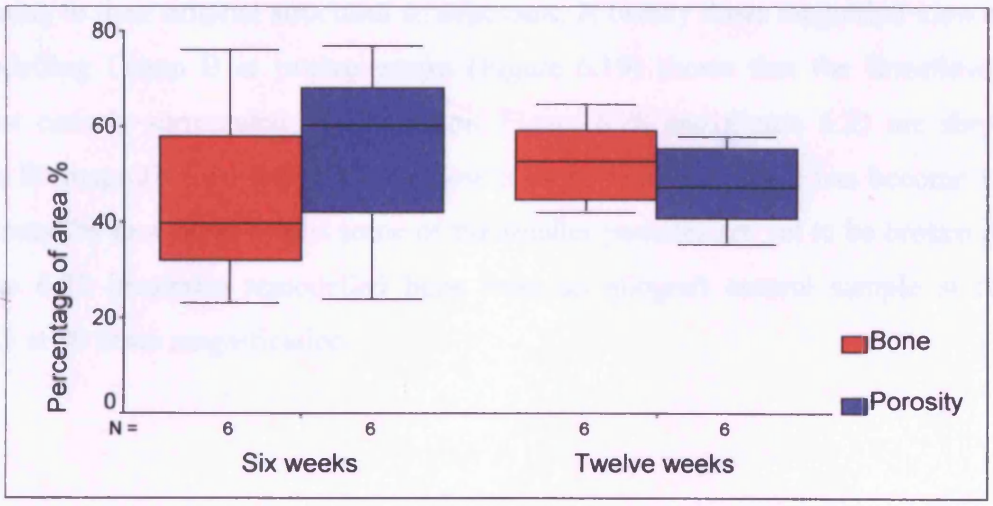

Figure 6.10 - Box plot of percentage of the defect containing bone or fibrous tissue for Group A at six and twelve weeks

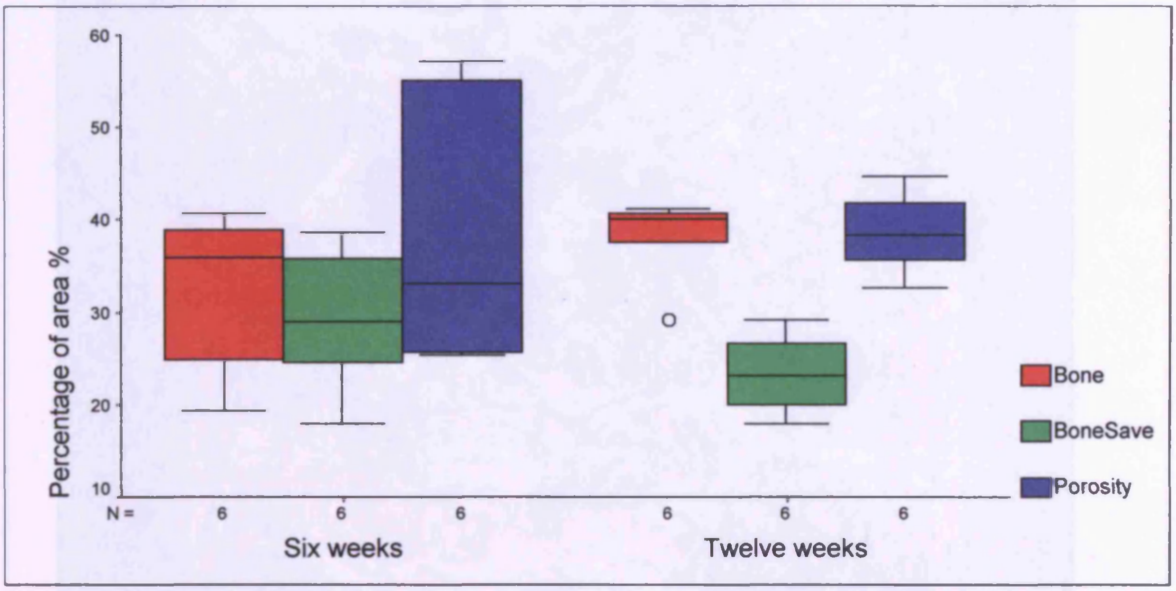

Figure 6.11 - Box plot of percentage of area containing Bone, BoneSave™ or fibrous tissue for Group B at six and twelve weeks

An impacted sample from each group at time Zero is illustrated in Figure 6.12 and Figure 6.13. Although the BoneSave™ particles are white, when photographed with the light behind them they show up bluey-grey. A twenty times magnified view (Figure 6.14) shows that the BoneSave™ particles have become crushed under the impaction and that only small elements of their initial porosity remain (in this picture the BoneSave™ is pinky white). Figures 7.15 to 7.18 illustrate the graft at six and twelve weeks post operative. By twelve weeks the trabeculae in Group A are showing signs of returning to their original structural arrangement. A twenty times magnified view of the remodelling Group B at twelve weeks (Figure 6.19) shows that the BoneSave™ is almost entirely surrounded by new bone. Figure 6.20 and Figure 6.21 are shown at times 80 magnification and illustrate how a large crushed granule has become totally infiltrated by new bone, whilst some of the smaller particles are yet to be broken down. Figure 6.22 illustrates remodelled bone from an allograft control sample at twelve weeks at 80 times magnification.

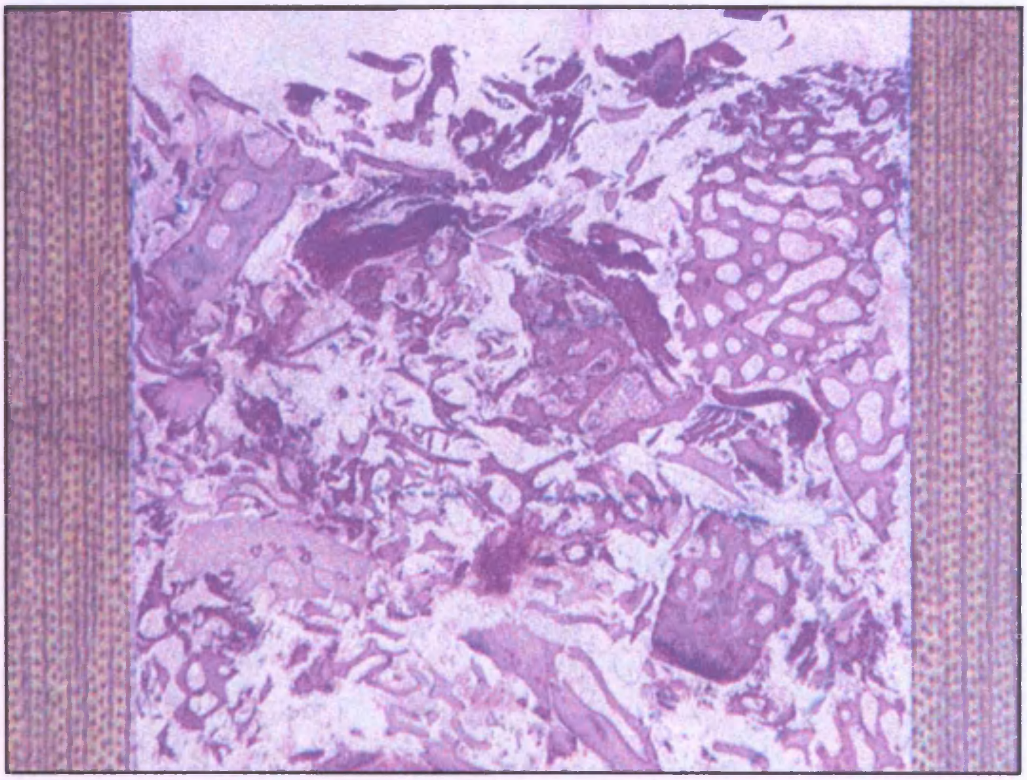

Figure 6.12 - Allograft sample at time zero (Magnification 6.7)

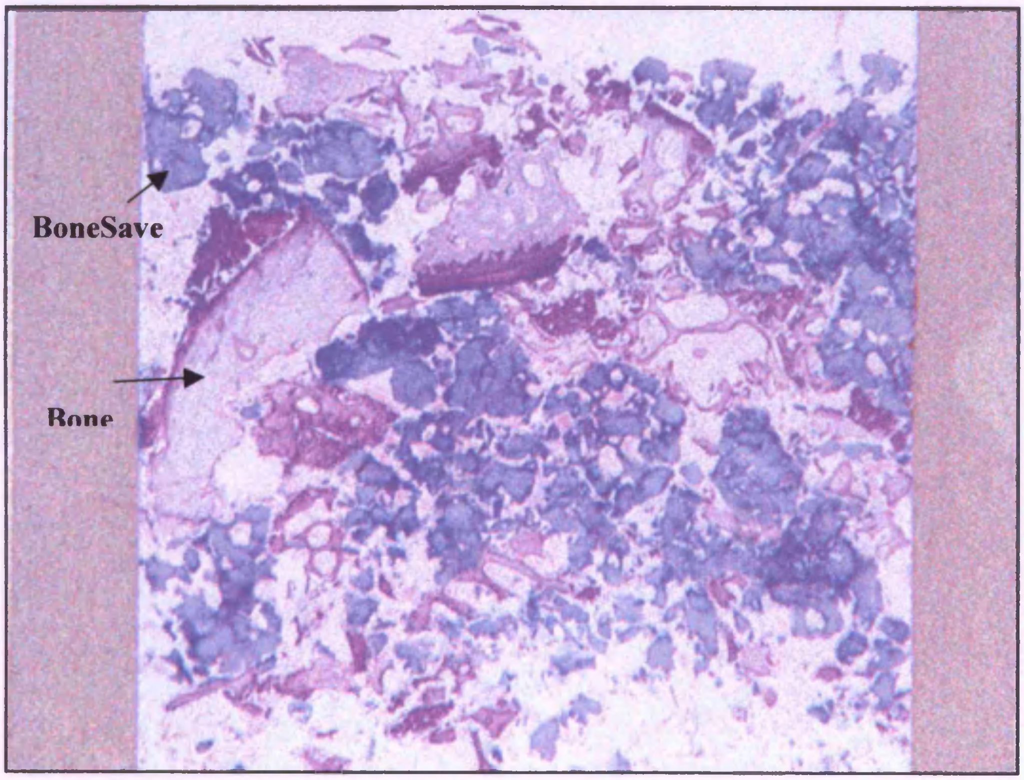

Figure 6.13 - Group B sample at time zero (Magnification 6.7)

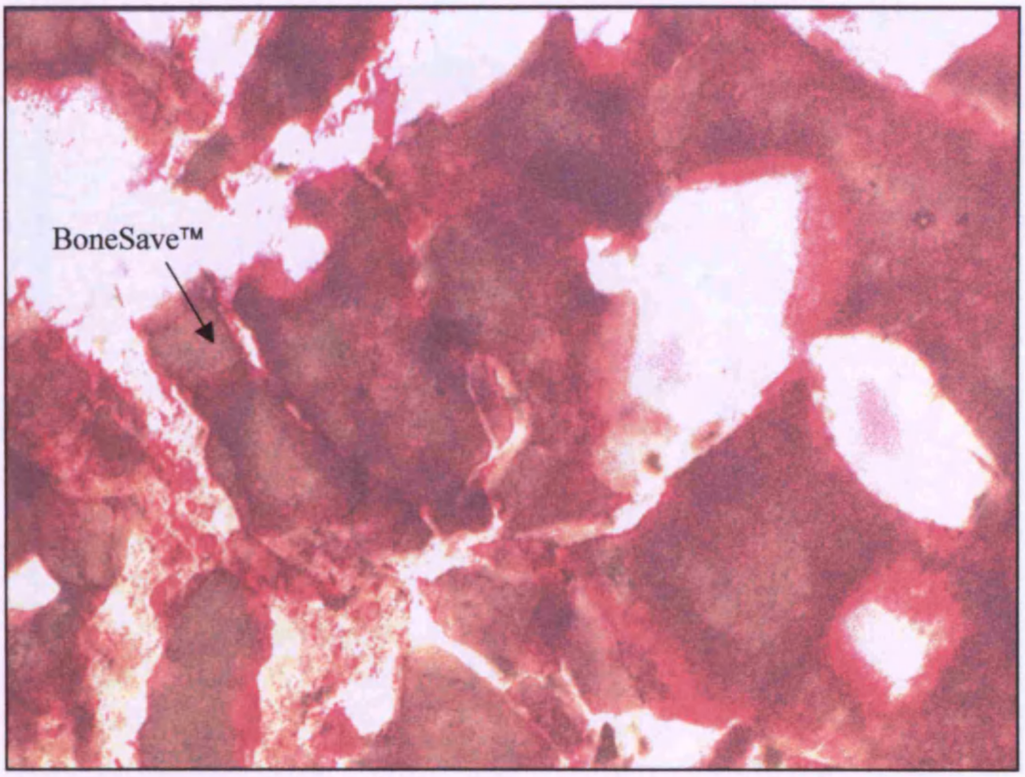

Figure 6.14 - Magnified BoneSave™ particle at time zero (Magnification x20)

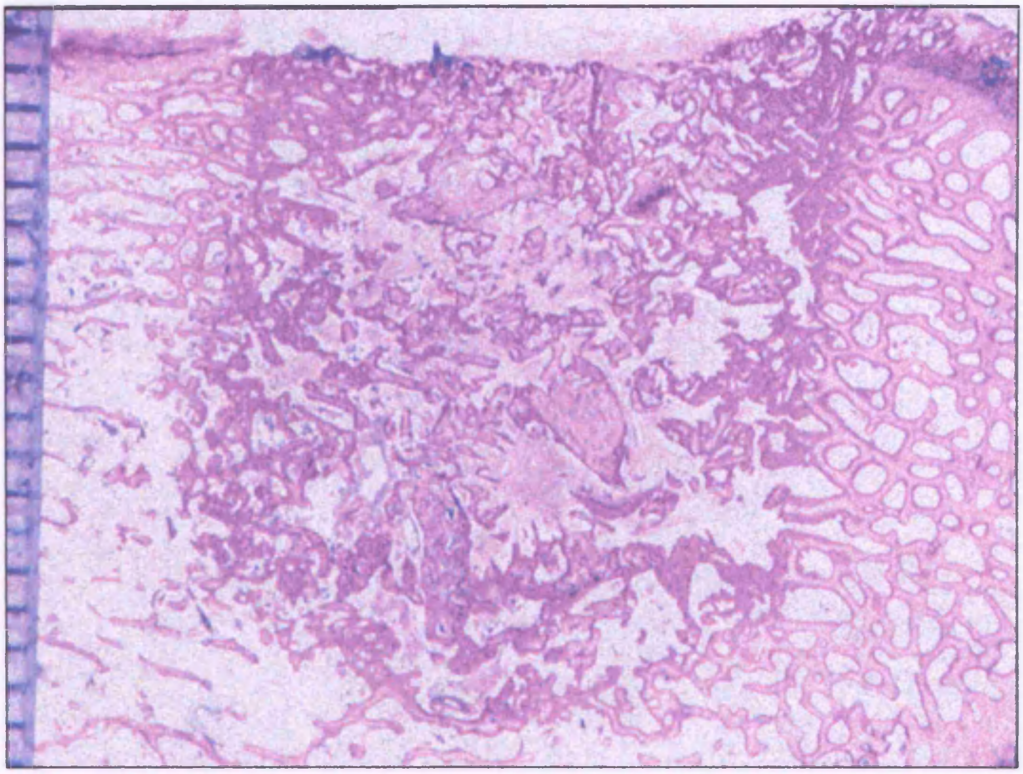

Figure 6.15 - Allograft at six weeks (Magnification 4.8). The darker stain indicates new bone

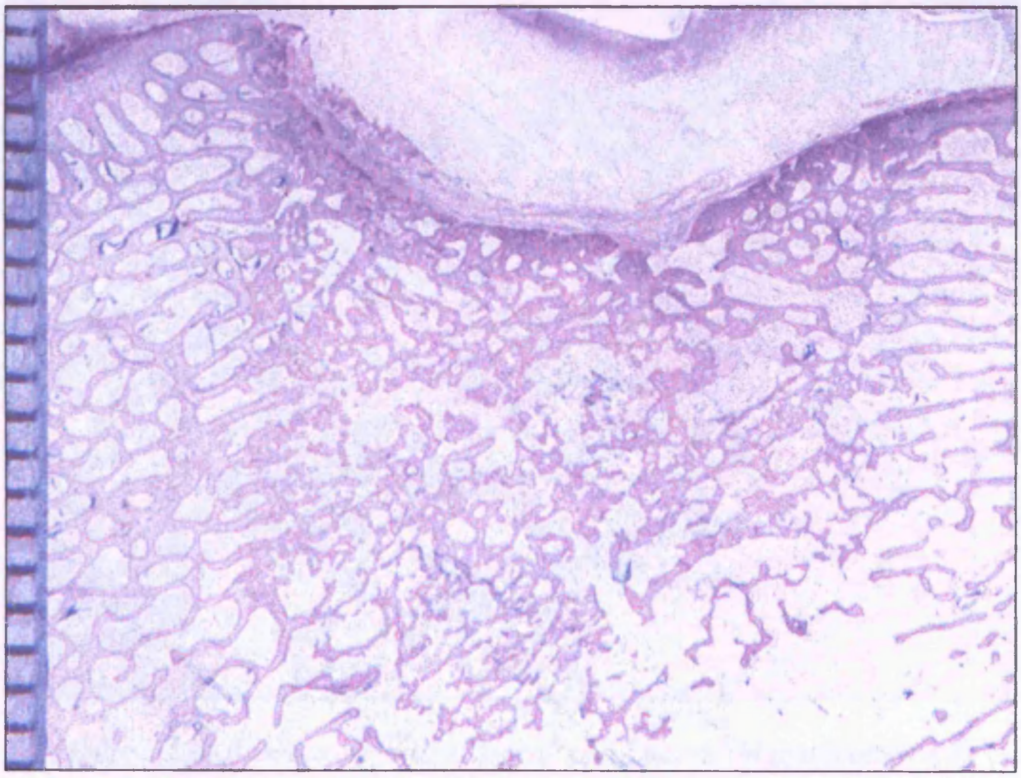

Figure 6.16 - Allograft at 12 weeks (Magnification 4.8)

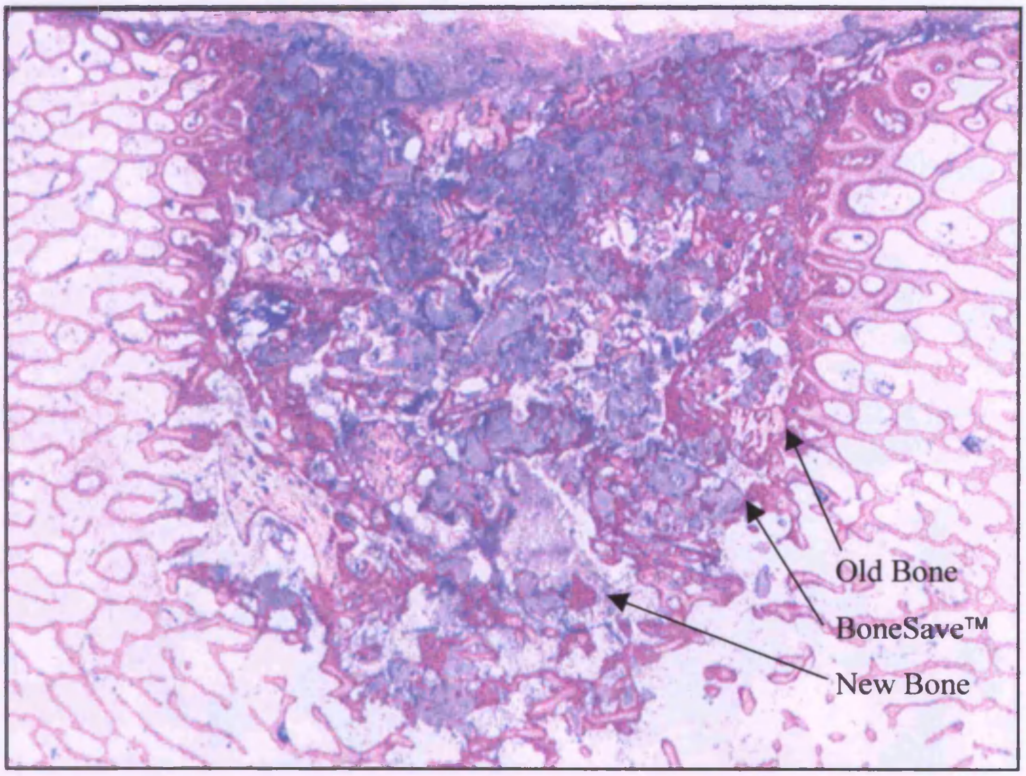

Figure 6.17 - BoneSave™ at six weeks (Magnification 4.8)

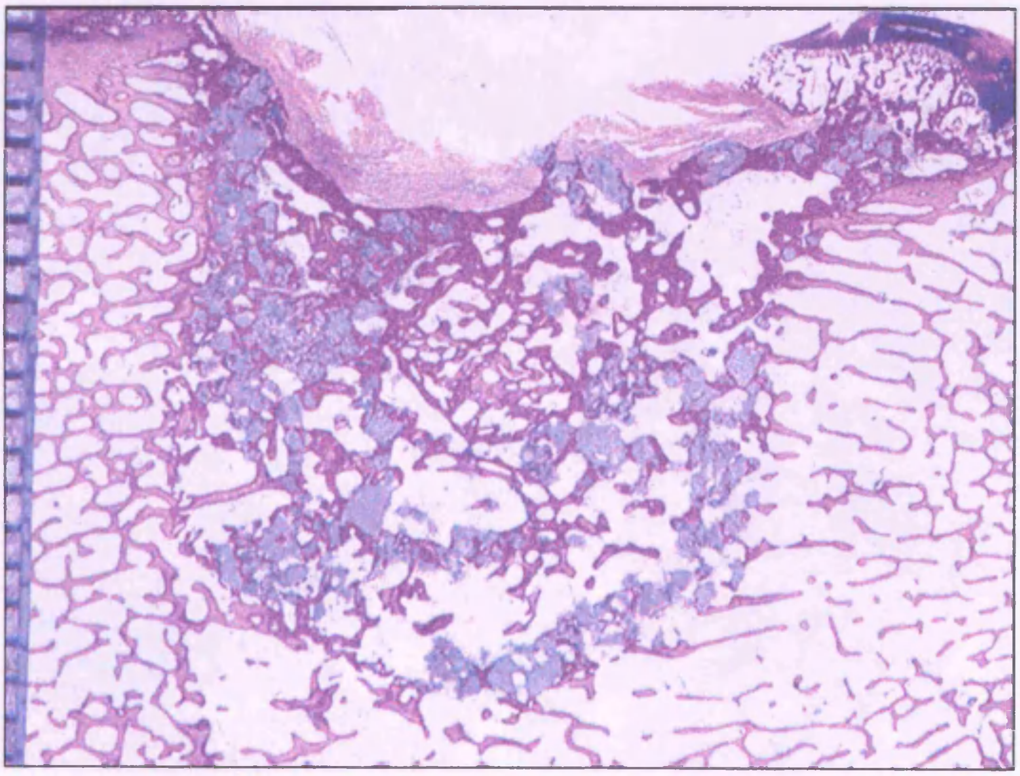

Figure 6.18 - BoneSave™ with allograft at 12 weeks (Magnification 4.8)

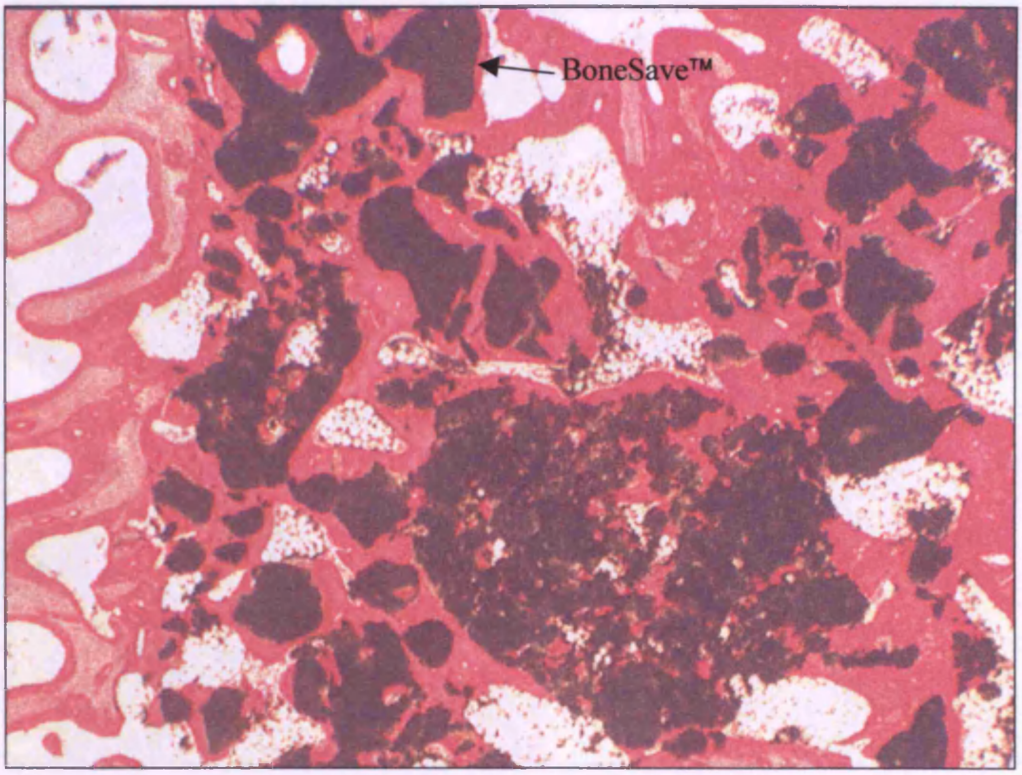

Figure 6.19 - BoneSave™ at 12 weeks (Magnification 20) BoneSave ™ shows as black

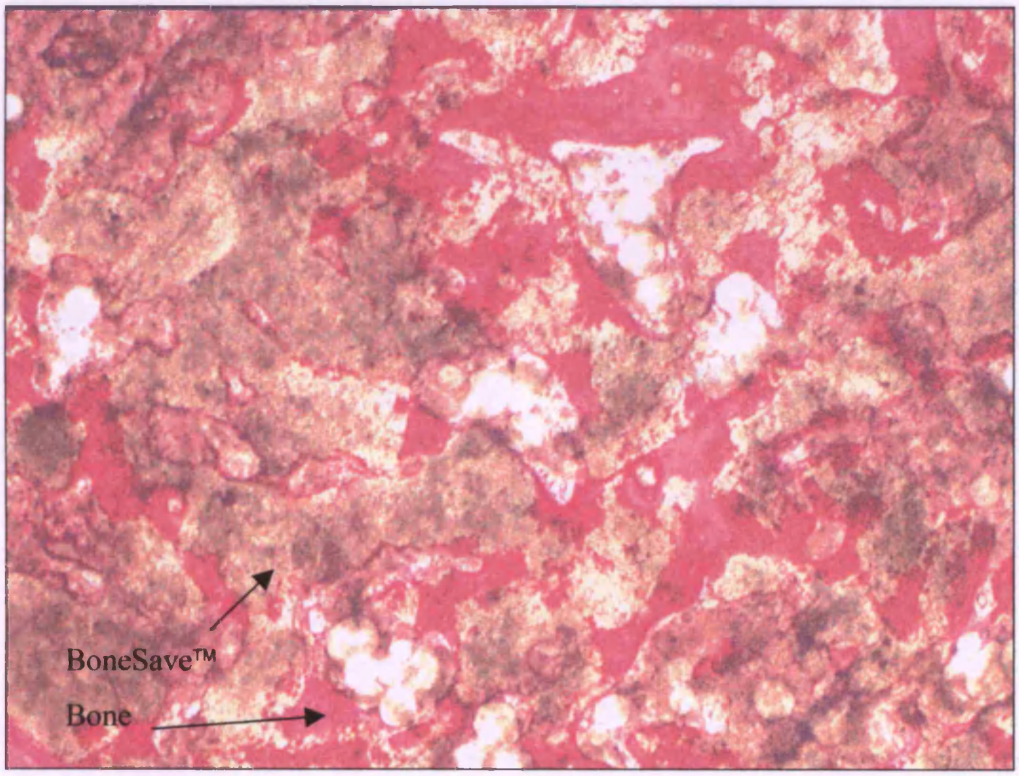

Figure 6.20 - BoneSave™ at 12 weeks (Magnification 80)

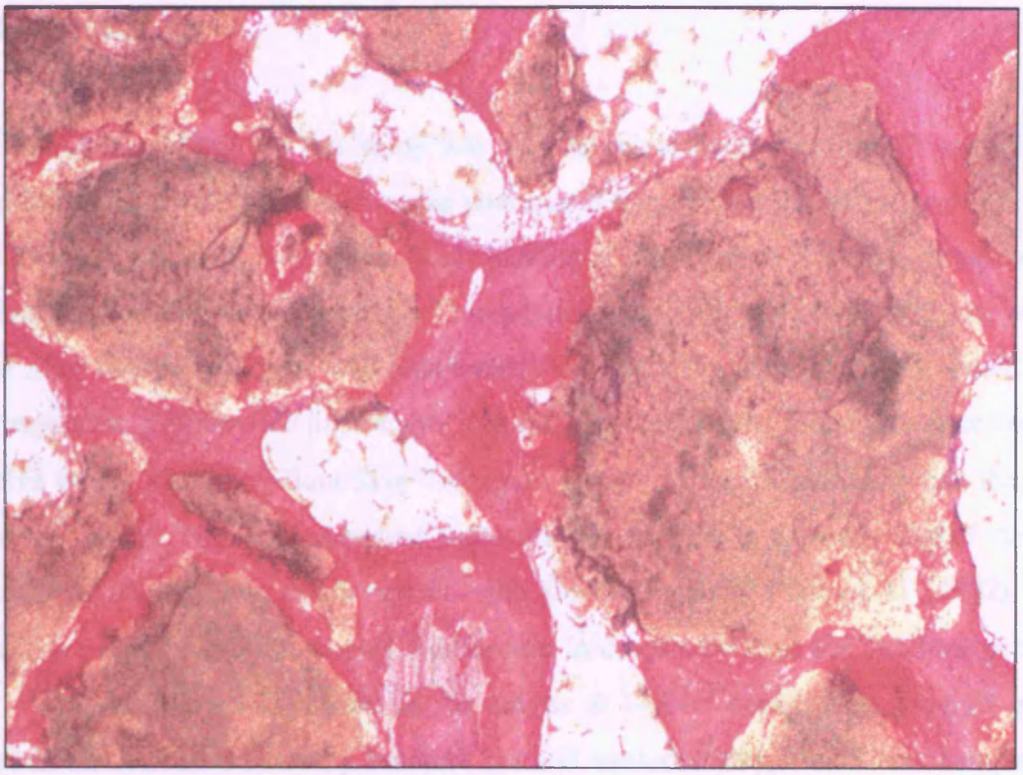

Figure 6.21 - BoneSave™ at 12 weeks (Magnification 80)

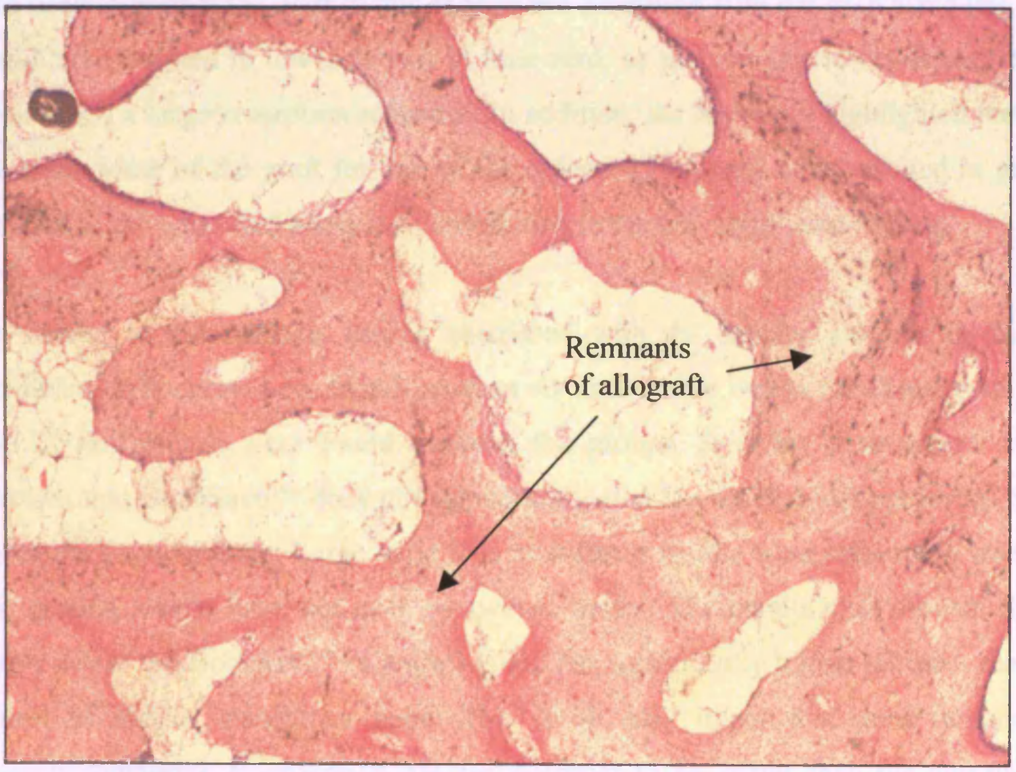

Figure 6.22 - Allograft at 12 weeks (Magnification 80)

6.4 Discussion

The initial hypothesis for this study was that the inclusion of BoneSave™ particles to morsellised allograft would reduce the anticipated drop in strength of the graft after six weeks of remodelling. A previous study looking at the affect of graft size, described in Chapter 5, found that the density of remodelling allograft was lower after six weeks than after twelve weeks. It was anticipated that this difference in density would also correspond to a difference in strength. The CT scanning results found that after six and twelve weeks, the 50:50 BoneSave™/allograft group had a higher density than the pure allograft group. This was expected since BoneSave™ has a naturally higher density than allograft and this result agrees with the findings of Pratt et al (2002). The BoneSave™ group did not display a difference in density between the two time periods, but it did have lower deviation in the results at twelve weeks. The allograft group showed an increase in density between six and twelve weeks, which was comparable with that in the graft sized study (Chapter 5). However unlike the graft sized study the difference was not significant. The possible cause for this result is that lower forces were used to impact the graft in this experiment compared with the graft sized test. This would have resulted in lower density at time zero, so perhaps this lower density didn't invoke such a large resorption response. In addition, the histology highlighted that in a few cases some of the graft fell out of the defect, which may have resulted in greater variation in the measured densities, contributing to the non significant finding.

The results of the stiffness testing correlated with the density analysis in that no significant differences were found between six and twelve weeks for either graft type. Also no differences were found between the groups, at either time period, which indicates that BoneSave™ does not significantly alter the mechanical properties of the graft during remodelling. Large variations in stiffness results were seen at six weeks in both groups, which were not seen by twelve weeks. The results also showed that at twelve weeks the BoneSave™/allograft group has significantly higher stiffness than the control of normal cancellous bone. This result may imply that once remodelled, allograft containing BoneSave™ has the potential to be stiffer than the surrounding cancellous bone.

The chosen loading regime for the mechanical test appears satisfactory as it gave repeatable results on the trabecular bone tested as a control. A small deviation in the stiffness of the control was expected, as the stiffness of trabecular bone will vary between animals and position down the femur. During testing, large differences were noted in the "toe region" of each test, which would have affected the results significantly if they had been displacement controlled. The "toe region" is where the impactor was coming into contact with the sample prior to performing the preconditioning cycles. This difference in the impactor's travel is due to varying visco elastic properties of the sample, and any minor discrepancies in the top or bottom surface of the sample. The stiffness test was non-destructive and had the yield point of each sample been reached, the findings may have been different. It is possible that other tissue within the sample, as well as the bone and BoneSave™, may have affected the mechanical stiffness. Tagil at al (2001) found that fibrous armouring of the graft increased its mechanical strength. Therefore it is possible that the mechanical stiffness observed in this study might be as a result of fibrous infiltration into the graft rather than remodelling. However, the histology sections did not highlight this to be the case.

The histology results are in line with those of Pratt et al (2002). After 14 weeks they found a quantity of bone in the allograft control group to be 55.6 ± 4.1 %, and in the 50:50 allograft /BoneSave™ group 40.4 ± 3.8 % bone and 42.6 ± 3.8 % BoneSave™. However our allograft control had higher variability, 52.7 ± 8.5 % bone at twelve weeks, which had an even greater standard deviation at six weeks: 44.9 ± 19.8 %. These high deviations might be due to graft falling out of some of the defects, whereas their defects were capped with cement to prevent this problem. At twelve weeks there was less BoneSave™ remaining in our defects 23.3 ± 4.1 %, compared with Pratt's at 14 weeks. Indeed, in Group B there was significantly more bone than BoneSave™ at twelve weeks, which was not the case at six weeks. There is no apparent reason for this difference compaired to Pratt's findings, but it does indicate that the BoneSave™ is being resorbed.

However it is important to note that this study was only testing BoneSave™ in a defect model, which would not have subjected it to the high loads that one would expect around a prosthesis.

A successful methodology for mechanical testing of remodelling impacted graft has been described above. However any future investigators wishing to pursue a similar technique may wish to consider the following. The impaction force of the graft played an important role in this study, high impaction may invoke prolific resorption prior to the remodelling. But graft impacted with low forces may to a greater or lesser extent fall out of the defect, creating high variation in the results. A possible solution is to include a cement cap, as described by Griffon et al and Pratt et al 2002, or to contain the defect with a mesh secured by either cerclage wires or screws.

6.5 Conclusions

This study has shown that BoneSave™ can be used as an extender to allograft without detrimental affects on density or mechanical strength. The stiffness of remodelling bone graft, on its own or mixed with BoneSave™, is more variable at six weeks than twelve weeks, although it is still similar to the surrounding cancellous bone. When BoneSave™ is used as a bone graft extender, the bone mineral density of the graft will be higher. This study was unable to prove the hypothesis that the mechanical stiffness of allograft would be lower at six weeks than at twelve weeks post implantation. Nor did this study find that the inclusion of BoneSave™ with the allograft chips increased the mechanical stiffness of the remodelling graft post operatively. Under an impaction force of 4 kN there was no significant drop in density or mechanical strength of allograft during remodelling. The remodelling BoneSave™ showed signs of resorption and being replaced by new bone by twelve weeks postoperative.

This study shows that BoneSave™ can be used as a bone graft extender as a 50/50 mix with allograft, without detrimental effects on the mechanical strength of the graft during the remodelling phase. To asses the ability of BoneSave™ to withstand the high compressive loading forces round a prosthesis a more realistic femoral model study is required.

Chapter 7

Mechanical Testing and micro section analysis of BoneSave™ in Cadaveric Femurs

7.1 Introduction

BoneSave™ is a combination of Tricalcium Phosphate and Hydroxyapatite (80:20 ratio). In the previous chapter a study into the mechanical strength of a 50:50 mix of BoneSave™ and allograft was conducted. This showed that the compressive stiffness after six and twelve weeks, in an in-vivo ovine model, was similar to 100% allograft. However, that study was only carried out on a small test sample and the graft was only subjected to load naturally travelling through the bone. Clinically the compressive forces applied to the graft around a femoral stem could be much higher.

Blom at al (2001) and Blom at al (2002) have performed studies on BoneSave™ in in-vitro and in-vivo femoral stem ovine models. However there is little to guarantee that their impaction method represents that found clinically and the loading pattern of a sheep is lower than in humans. Thus it was decided that a study to prove the mechanical integrity of 50:50 BoneSave™ / allograft at time zero should to be performed, with a realistic representation of the surgeon's impaction grafting technique and the subsequent loading forces.

BoneSave™ was impacted as a 50:50 ratio with allograft in the right of seven pairs of cadaveric femurs with allograft used in the left femurs as a clinical control. A surgeon who uses impaction grafting in surgery conducted the impaction procedure. To evaluate the consistency of the surgeon and the affect of the BoneSave™ on his technique, the impaction forces for each test were measured using the modified hammer discussed in Chapters 2 and 3. The impacted femurs were subjected to a series of cyclic loading in a hydraulic machine, and the subsidence of the stem measured to assess the influence of BoneSave™.

BoneSave does not compress in the same way as allograft since it does not have the visco elastic properties, and it is more brittle. Consequently the two types of impacted graft may have a different physical appearance. So to determine the level of impaction of the graft types histological analysis was performed on the cadavers after mechanical testing. The analysis of the control group enables further evaluation of Femoral Impaction grafting in general, as well as specific to this study. Since the distal impactors have a smaller surface area compared with the proximal impactors it is likely that for similar forces they will create higher pressure. Therefore it is possible that the graft will be more compacted distally. Also the mechanical loading of the graft may also add to this making the distal graft less porous.

Hypothesis

Addition of 50% BoneSave™ to 50% allograft will improve the mechanical properties at time zero. The empty space (void of bone or BoneSave™) will be lower in the cadavers impacted with a 50:50 mix of allograft and BoneSave™ than allograft. A greater level of impaction will be observed in the cadavers distally to proximally.

The study was conducted at the Department of Physics and Medical Technology, Vrije Universiteit Medical Center (VUMC), Amsterdam, The Netherlands. I was not involved in the initial design of the mechanical testing. However I was present for all surgical procedures and the mechanical testing. I did not perform the analysis of the mechanical testing. My role during the surgery was to measure the surgeon's impaction forces and to analyse these results. Once the mechanical testing was complete the bones were transferred to The Centre for Biomedical Engineering, Institute of Orthopaedics, University College London, UK, where I performed all histology sectioning and analysis.

7.2 Methods

Seven matched pairs of cadaveric femurs were used in this study. There were variations in size between specimens, but not between left and right of each pair. Left femurs were used in Group A, indicating the use of allograft, right Group B, indicating the BoneSave™ / allograft mixture. The cadavers had been frozen and fixed in formal saline prior to the start of this study.

7.2a Preparation of the graft

To create the allograft fresh frozen donor femoral heads were obtained from the bone bank of the Department of Orthopedics of the VUMC that had been stored at -80°C for at least 6 month. The cartage was removed from the heads prior to milling in a Tracer Bone mill, with the large rasp (Zimmer, Santa Paula). The morsellised allograft was ready for use in Group A and to create the Group B graft, equal quantities by weight of BoneSave™ and allograft were mixed (Figure 7.1). The number of bones being operated on in a day determined the required graft quantities that were prepared.

Figure 7.1 - Preparing the BoneSave™ / allograft mix

7.2b Surgical Procedure

The surgeon impacted each pair of femurs consecutively, performing on the control side first then the experimental side. The first pair of femurs where done on one day, femurs 2 & 3 were done on the same day a week later, femurs 4, 5 & 6 another week later and femur 7 was done on its own a week after that.

The Exeter X-change technique[1] was followed as closely as possible. The Exeter Revision instruments[1] were used to perform the surgical procedure with the addition of the modified Exeter slap hammer (Chapters 3 and 4), which enabled impaction forces to be recorded and analysed on a laptop computer. Standard revision materials[1] were used for the operations *in vitro*. These consisted of a bone plug, a central guide wire, Simplex bone cement and Exeter stems.

To mimic the situation at revision the femoral head was cut off and the cancellous bone rasped away. A femoral plug was pushed down the canal, to a position 20 mm distal of the major trochantor in all femurs. The grafting procedure involved hammering the graft down the femoral canal with increasing diameter distal impactors (distal impaction). Once the cavity was about two thirds full, a proximal impactor was rammed into the graft (proximal impaction), which created the space for the implant to be cemented into. Figure 7.2 shows a cadaveric femur impacted with the allograft / BoneSave™ mix prior to cementing a stem into place. The selection of the Exeter femoral stem size was chosen as that which easily fitted into the shaft, left and right of each pair receiving the same size. Although the forces were recorded during the grafting process, they were not instantaneously available to the surgeon. Consequently the surgeon used his experience and "feel" to determine when the graft had been compacted enough. The recorded forces were placed into two groups, distal and proximal impaction, and analysis performed.

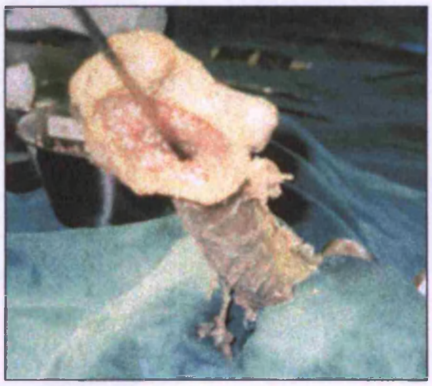

Figure 7.2 - Cadaveric bone filled with BoneSave™ / allograft mix

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[1] Stryker® Howmedica Osteonics, Raheen Business Park, Limeric, Ireland.

7.2c Mechanical testing

After the surgical procedure, the distal ends of all the femora were embedded in a low melting point alloy with the artificial head positioned precisely above the center of the knee joint. To test mechanical stability the femora were placed in a hydraulic material testing device[1] and loaded under a compressive sinusoidal force of 400 to 2,000 N. This load was applied by a flat plate, allowing a horizontal shift of the femoral head under bending of the specimen (Figure 7.3). The loading frequency was 6 Hz and all specimens underwent a total of 50,000 cycles, with a rest period of 5 minutes after the 1,000 and 10,000 cycle. The rest periods were used to quantify total deformation and its components elastic and plastic deformation. The elastic deformation was defined as the amount of recovery during the rest period. By subtracting the elastic deformation from the total deformation, the subsidence was calculated.

Figure 7.3 - Mechanical testing of the femurs

[1] Instron 8872, Instron® Corporation, Canton, MA, USA

7.2d Imaging

Radiographs were made before and after preparation of the femur, after the surgical procedure and after cyclic loading. Plain photographs of the femora are taken to document the operation procedure and the failure mechanism. Before surgery a DEXA scan (QDR-2000®, Hologic Corporation, Waltham, Mass), using an Array Left/Right Hip protocol, was made of all the femora. This was done to objectify the Bone Mineral Density (BMD), so if a failure occurred this could possibly be explained by a low quality of the bone tissue.

7.2e Histology analysis

After the mechanical testing the femurs were embedded and sectioned, using a similar process to that described in Section **5.2h**. However chloroform dissolves cement so a 50:50 mix of methylated spirit and diethyl ether[1] was used as an alternative to defat the bone. Since the samples were larger, the time spent in each stage of processing was increased. Prior to embedding, the number of each specimen was etched on to the visible area of the prosthesis. To assist with the penetration of resin during embedding, it was necessary to remove the un-required distal end of the femur and cut slots in shaft. Positions of the slot were chosen so that they did not interfere with the desired sectioning sites. Three sections (distal, medial and proximal) were cut from each cadaver for analysis. The distal cut was taken just above the tip of the prosthesis, while the medial and proximal cuts were approximately 50 mm and 100 mm above that. The slides were stained with paragon (25mins).

To measure the cement mantel, pictures were taken of each section using the JVC camera and zoom lens (with the slides on a light box) and analysed with KS300. For the proximal and medial sections 24 measurements of the cement mantel thickness were taken around the stem: six on the anterior side of the stem (Position A), six on the medial side of the stem (Position B), six on the posterior side (Position C) and six on the lateral side (Position D) as shown in Figure 7.4. Twenty four measurements were also taken around the stem on the distal sections. However the stem is almost circular at the tip so no reference could be made in relation to position round the stem.

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[1] BDH Laboratory supplies

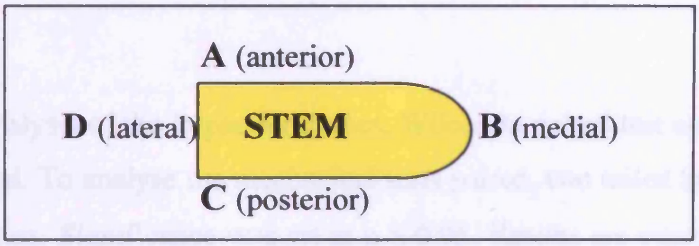

Figure 7.4 - Measurements around the stem

To measure the percentage of bone and BoneSave™ for each slide, they were mounted in the Olympus microscope, with a 10 x 10 mm Graticule[1] in the eyepiece. Several areas of the bone were examined at times 4 magnification. The line intersect method was then used, with the graticule, to determine the percentage of BoneSave™, bone or unoccupied area (normally soft tissue and fat).

[1] Graticules Ltd. Tunbridge, Kent, UK.

7.3 Results

For statistical analysis of the impaction forces, Wilcoxon paired test and Mann-Whitney U tests were used. To analyse the mechanical tests paired, two tailed Student t-test were used for all femurs. Significance was set at $p \leq 0.05$. Results are expressed as averages ± standard deviations.

7.3a Surgical procedure

In two pairs of femurs a Size 0 stem was used and in five pairs of femurs a Size 1 stem was used. In cadaver numbers 1, 2 and 4 operated with BoneSave™, a fracture developed during the proximal impaction procedure. No fractures occurred in the 100 % graft group. The fractures were treated with three cerclage wires around the proximal cortex of the femur, after which the operation procedure was continued as normal. The mean (± SD) amount of graft used in Group A was 75.1 ± 11.0 grams, and in Group B 70.7 ± 11.3 grams (Table 7.1). The amount of graft, by weight, in the 100% graft group was significantly higher than in the BoneSave™ group ($p = 0.05$).

Femur No	Group A (g)	Group B (g)
1	88.3	78.6
2	62.9	52.1
3	67.3	62.6
4	65.1	64.8
5	74.5	76.4
6	77.3	76.2
7	90.6	84.5
Average ±SD	*75.1 ±11.0*	*70.7 ±11.3*

Table 7.1 - Quantities of graft used in each femur, in grams

7.3b Impaction Forces

The results have been collated in Table 7.2 to show the number of impacts in each group, their average force, with standard deviations, and the collective sum of all the forces in each group. The sum off the forces gives an indication of the energy put into the impaction, since it is possible that if the surgeons average force is low for any given femur, he may have found it necessary to impact more times prior to obtaining a stable graft bed. Unfortunately some data was lost during the recording of the distal impaction forces in Femur 6B.

Femurs	1		2		3		4		5		6		7	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**
No. of distal impacts	160	139	119	122	122	185	114	211	134	143	100	90	114	129
Sum of distal forces (kN)	2518	3046	1152	1369	1276	1311	1263	2597	1599	1606	1571	1053	1202	1816
Average distal force (kN)	15.7	21.9	9.7	11.2	10.5	7.1	11.1	12.3	11.9	11.2	15.7	11.7	10.5	14.1
Standard deviation	4.0	7.4	3.6	2.8	2.3	2.2	3.8	3.8	2.4	2.5	5.7	4.1	3.4	4.3
No. of proximal impacts	120	118	195	153	92	71	185	107	69	129	15*	62	74.0	185
Sum of prox. forces (kN)	2570	2896	3459	1698	985	474	2326	1048	721	1312	179*	492	568	1427
Average prox. force (kN)	20.4	24.5	17.7	11.1	10.7	6.7	12.6	9.8	10.5	10.2	13.1	7.9	7.7	7.7
Standard deviation	7.0	6.2	7.3	4.1	4.2	1.4	2.5	5.4	2.1	3.6	3.4	1.3	2.4	2.3
Total no. of impacts	280	257	314	275	214	256	299	318	203	272	115	152	188	314
Sum of all impacts (kN)	5089	5942	4612	3067	2261	1786	3589	3645	2321	2918	1767*	1545	1770	3243
Average force (kN)	17.8	23.1	14.7	11.2	10.6	7.0	12.0	11.5	11.4	10.7	15.4	10.2	9.4	10.3
Standard deviation	6.0	7.0	7.3	3.6	3.2	2.0	3.1	4.5	2.4	3.1	5.5	3.7	3.3	2.2

Table 7.2 - Impaction forces from each groups

A box plot of distal impaction forces for all femurs is illustrated in Figure 7.5, and Figure 7.6 shows the proximal impaction forces. Over half (57%) of the data groups were not normally distributed, so only non-parametric tests could be performed on the data. No significant difference between Groups A and B was found for the average distal forces or average proximal forces when using Wilcoxon paired tests ($p>0.05$). There was also no significant difference between the average distal force and average proximal force within the groups ($p>0.05$). However Kruskial-Wallis tests performed on the seven femurs in each group for distal and for proximal impaction showed that at least one set of forces is significantly different form the others. When looking at the

* Unfortunately a technical error resulted in the loss of some of the distal impaction forces in Femur 6B.

distal and proximal impaction force box plots (Figure 7.5 and Figure 7.6) we can see that more force was used on the first femur in each group, particularly in the experimental group. Mann Whitney U tests of femur 1 with the rest in the group show a significant difference ($p<0.0001$). It may also be observed that in the control side significantly larger forces were used in the distal impaction on femur 6 and in the proximal impaction of femur 2. This variability may be due to the size of the femur or possibly that there was a learning curve in the technique.

Figure 7.7 and Figure 7.8 illustrate the sum of all the forces the surgeon used on each femur. There was no difference in the sum of forces between the two groups with the Wilcoxon paired test ($p>0.05$). Figure 7.9 is a boxplot of the average forces in each group, the range of which is larger for the control femurs than for those in the experimental group. In the BoneSave™ group femurs 1 and 3 have been highlighted as outlyers, again it is femur 1 that appears to have been impacted using greater forces than the others.

To compare the surgeons force used in this study, with that used in surgery, the forces used to impact graft were measured in one of his revision cases (Chapter 4 – case B/6). For the case the surgeon chose to use a long stem. With a long stem the distal plug was still placed 20mm distal from the anticipated position of the tip of the stem. Two hundred and ninety three distal impacts were recorded with an average force of 21.8 kN. This average matched that of the impacts used in femur 1B, although the number of distal impacts is greater than those used in all of the femurs in the study. The increased number of impacts in this case was probably because it was a long stem revision with distal osteolysis, so a greater quantity of graft had to be impacted distally. The femur in this case had severe proximal osteolysis, which required a large mesh. Due to the condition of the proximal femur only a few proximal impacts were used, after which the surgeon tapped the graft between the mesh and stem using hand held shaped impactors. Unfortunately these forces were not recorded.

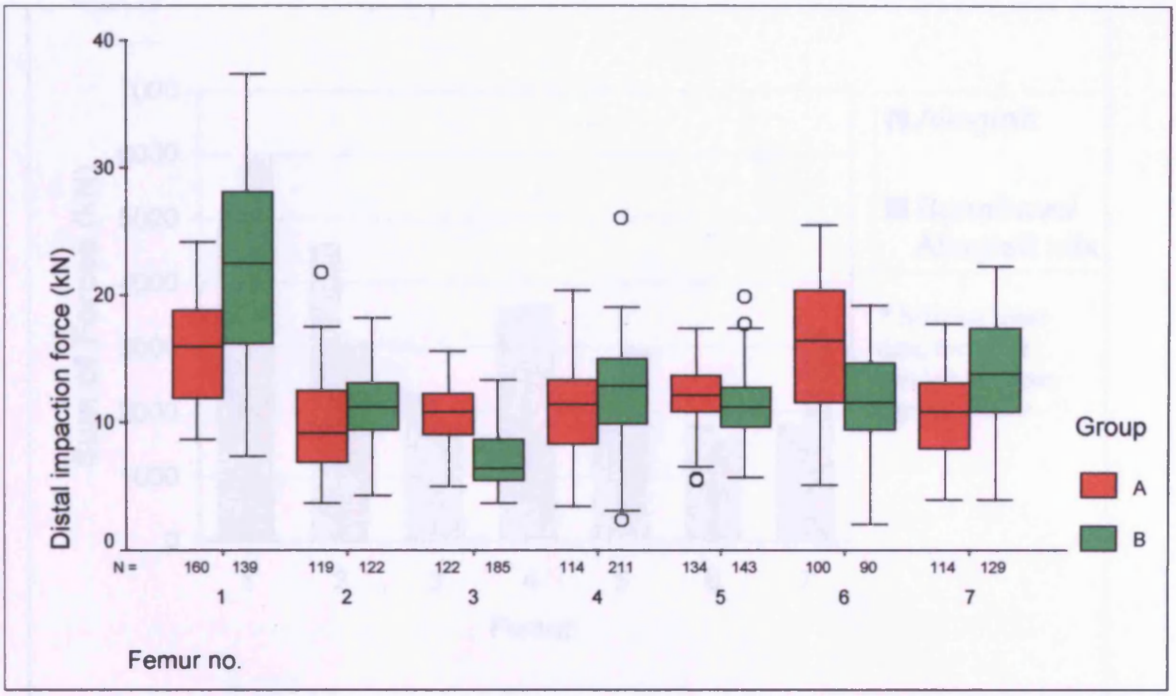

Figure 7.5 - Box plot of distal impaction force

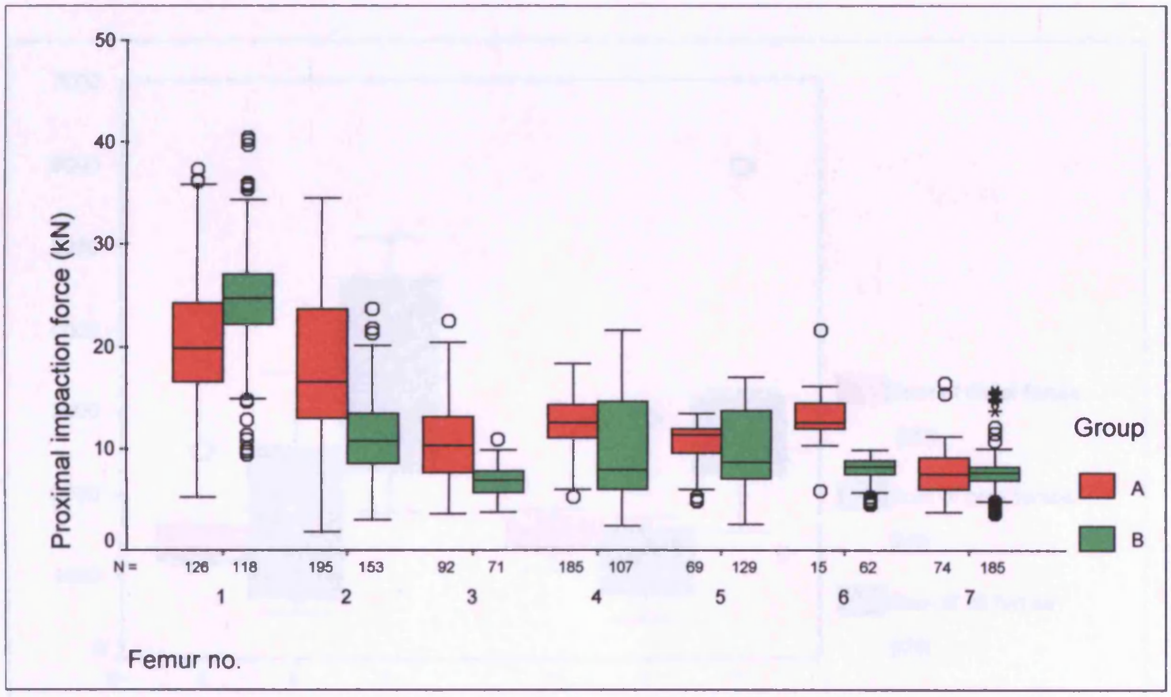

Figure 7.6 - Box plot of proximal impaction forces

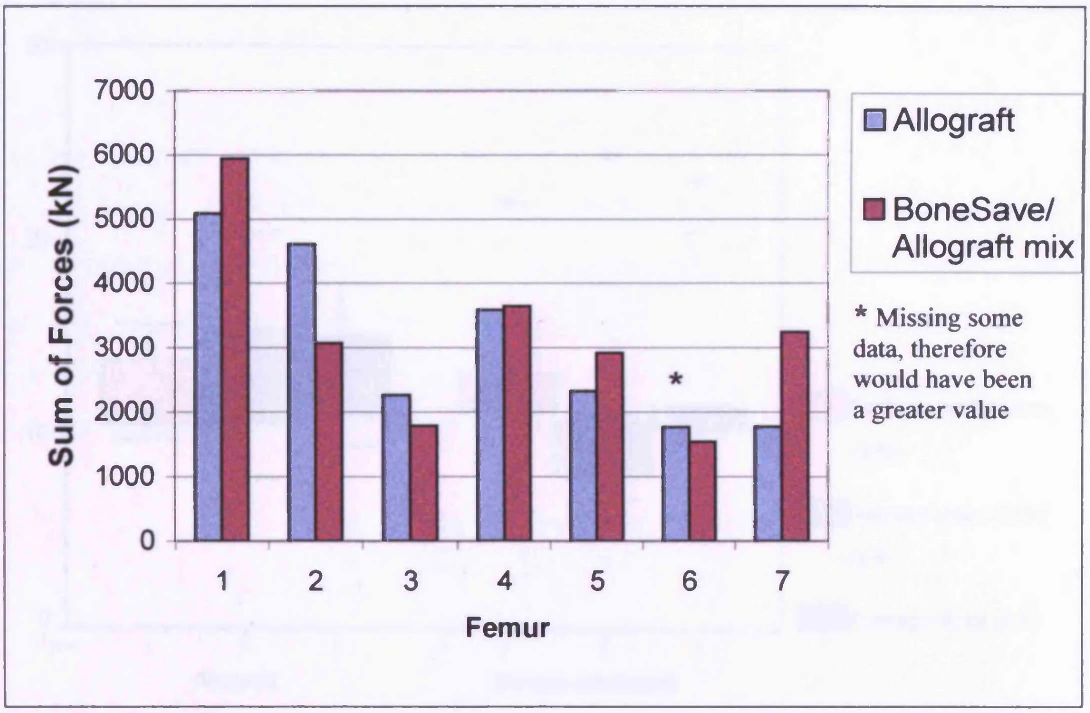

Figure 7.7 - Chart illustrating the sum of all forces for each femur

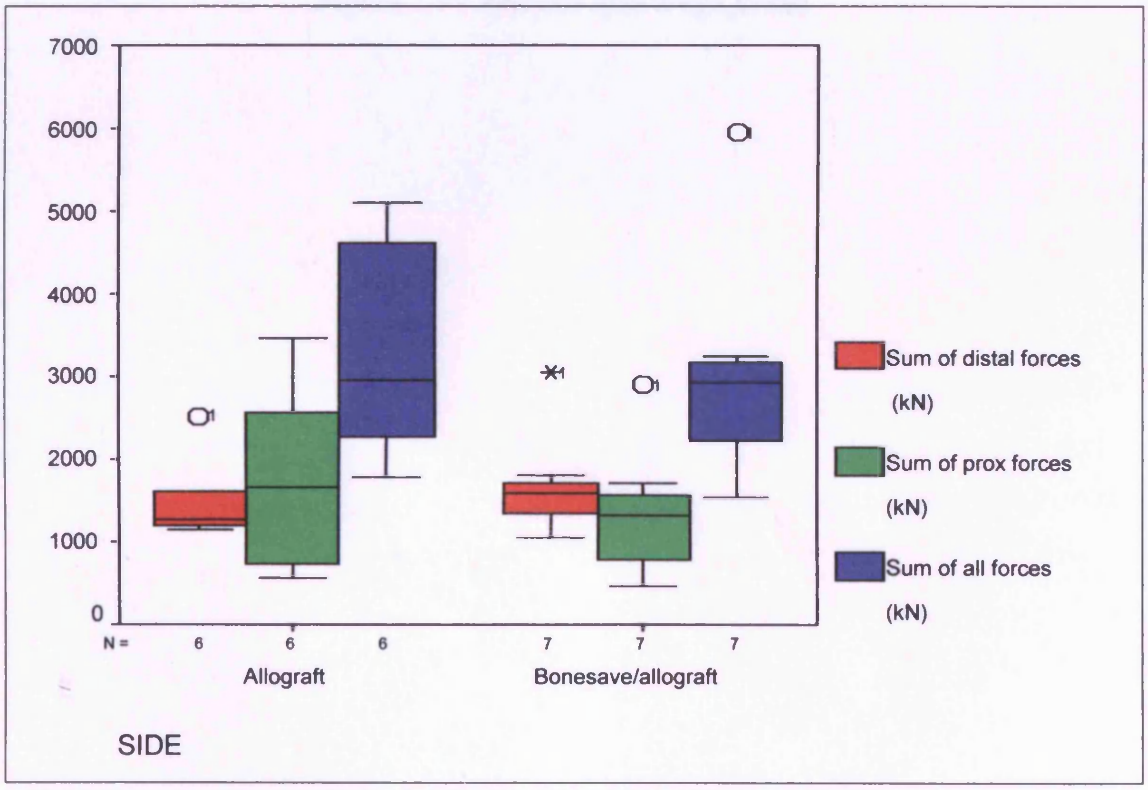

Figure 7.8 - Analysis of addition of all forces.

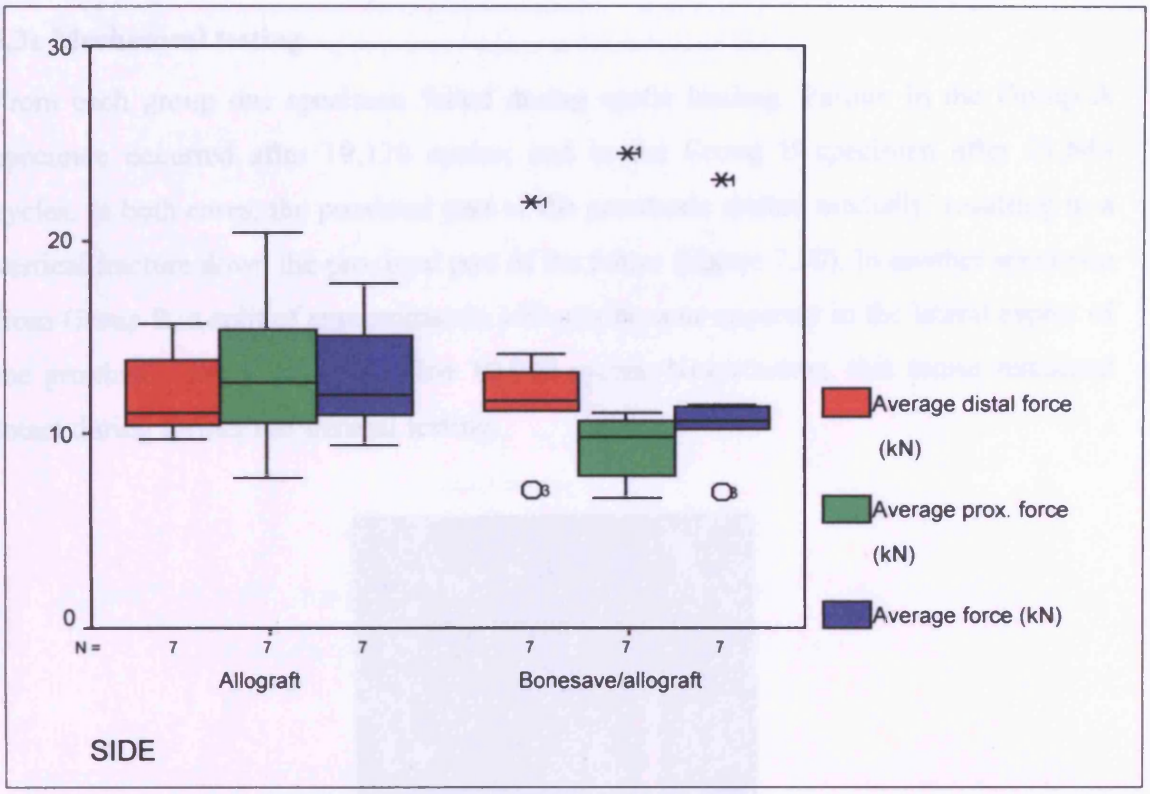

Figure 7.9 - Analysis of average forces

7.3c Mechanical testing

From each group one specimen failed during cyclic loading. Failure in the Group A specimen occurred after 19,120 cycles; and in the Group B specimen after 21,644 cycles. In both cases, the proximal part of the prosthesis shifted medially, resulting in a vertical fracture down the proximal part of the femur (Figure 7.10). In another specimen from Group B, a split of approximately 100 mm became apparent in the lateral aspect of the proximal femur during the first 10,000 cycles. Nevertheless, this femur remained intact during further mechanical testing.

Figure 7.10 - Failure of a specimen during mechanical testing

Most of the subsidence occurred during the first part of cyclic loading, after that the curves level off to a more constant level (Figure 7.11). In eleven of the fourteen specimens the plastic deformation was greater in the first 1,000 cycles than it was between the 1000 to 10,000 cycles (Table 7.3).

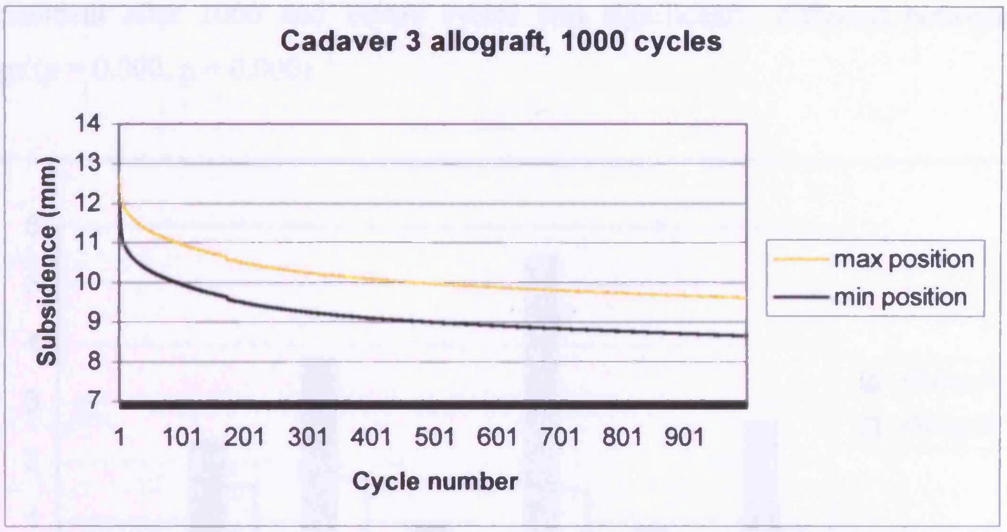

Figure 7.11 - Representative subsidence graph, illustrating that the most of the subsidence occurs during the first part of the test run

	1		2		3		4		5		6		7	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Subsidence from 0 to 1,000 cycles (mm)	0.11	0.11	1.93	1.10	2.52	0.80	0.49	0.25	3.93	0.75	0.43	0.27	1.48	0.53
Subsidence from 1,000 to10,000 cycles (mm)	0.03	0.11	0.41	0.49	1.21	0.92	0.40	0.24	1.60	0.79	0.41	0.22	1.22	0.34
Remarks		†		†		*		†		$			#	
† Fracture during surgery ** Failure at 9120 cycles* *$ Split down the shaft in first 10 ,000 cycle* *# Failure at 11644 cycles*														

Table 7.3 - Subsidence of the stem in mm during the first 1,000 cycles and from the 1,000 to 10,000 cycles during mechanical testing

The femurs reconstructed with 100% allograft produced higher subsidence after 10,000 cycles (Figure 7.12). Average subsidence in the control group was 2.31 ± 1.89 mm and 0.99 ± 0.62 mm in the experimental group. This difference was statistically significant ($p = 0.048$). Also, the femurs of the control group demonstrated greater variation in subsidence as shown by a higher standard deviation (Table 7.1). The ratio of the average subsidence of the control over the experimental group is 2.34. This indicates that subsidence was more than two times greater in the experimental group. The total displacement after 1000 and 10000 cycles was significantly different between the groups (p = 0.000, p = 0.000)

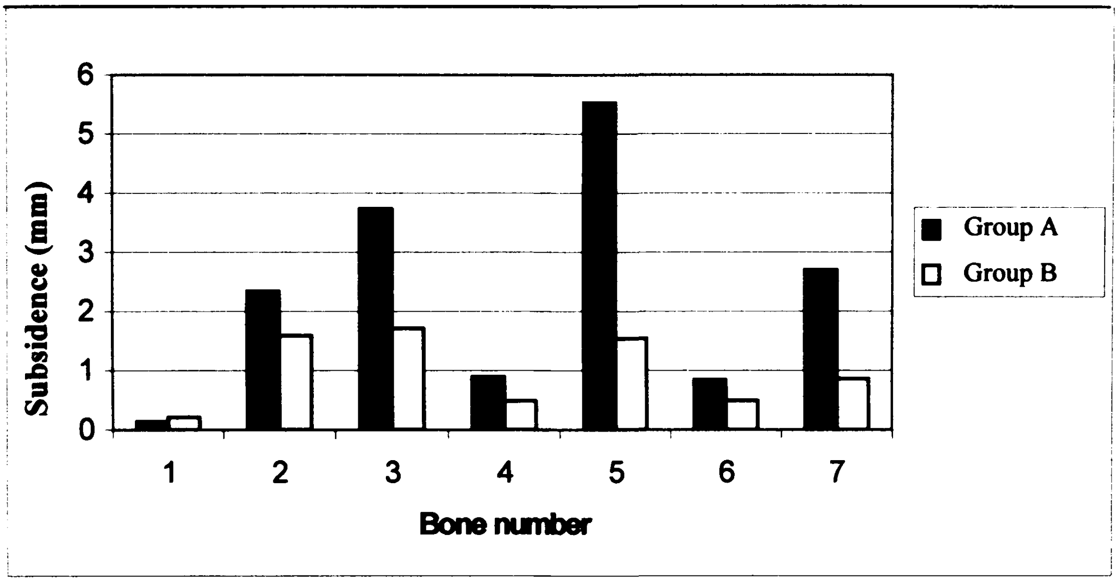

Figure 7.12 - Subsidence of the prosthesis after 10,000 cycles for Groups A and B.

Bone number	Group A	Group B	Ratio A/B
1	0.13	0.21	0.63
2	2.34	1.59	1.47
3	3.74	1.72	2.18
4	0.89	0.49	1.82
5	5.53	1.54	3.59
6	0.84	0.49	1.72
7	2.69	0.86	3.12
Average ±SD	*2.31 ±1.89*	*0.99 ±0.62*	*2.34±1.00*

Table 7.4 - Subsidence in mm and ratio of Group A to Group B after 10,000 cycles

Elastic deformation of the specimens was calculated at the end of each 5-minute rest period. After the 1,000 and 10,000 cycles the elastic deformation in the control group was higher than in the experimental group. Furthermore, the elastic deformation values of the control group after 10,000 cycles were associated with higher standard deviations, indicating greater variability in the elastic deformation in this group (Table 7.5).

No. of Cycles	Elastic Deformation (Average ± SD, mm)	
	Allograft	Allograft/BoneSave™
1,000	0.34 ± 0.21	0.26 ± 0.21
10,000	0.49 ± 0.43	0.38 ± 0.30

Table 7.5 - Average elastic deformation ± SD, in mm, after 1,000 and 10,000 cycles

7.3d Imaging

The average total Bone Mineral Density (BMD) ± the standard deviation in the control group was 0.762 ± 0.186 grams/cm^2 and 0.742 ± 0.177 grams/cm^2 in the experimental group. There was no statistically significant difference between the two groups. There is no relation between a low BMD and the occurrence of failures during surgery or mechanical tests. All postoperative radiographs showed well-positioned prostheses (Figure 7.13).

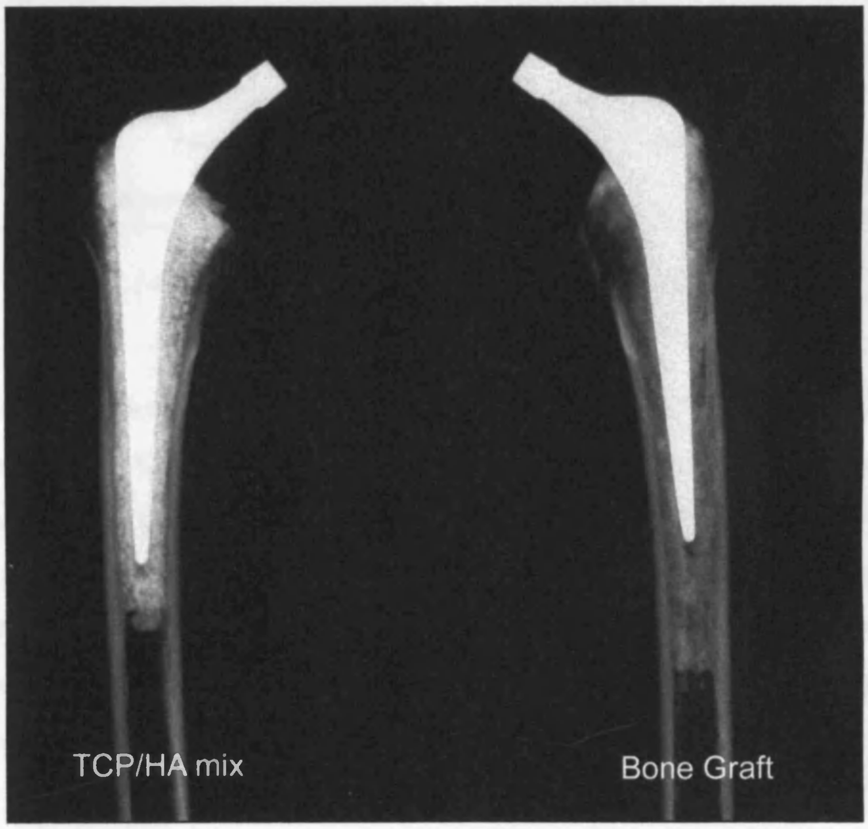

Figure 7.13 - X-ray after mechanical testing. At the left side a mix of BoneSave™ and allograft is used for reconstruction of the bone defect. At the right side solely allograft is used. At both sides the prosthesis is well positioned

7.3e Histology

Four pairs of cadavers were sectioned for histology, Numbers 1, 2, 4 and 6, along with Femurs 3A, 5A and 7B. The other specimens were too badly damaged during mechanical testing to be sectioned. Analysis was performed on the paired data using Wilcoxon test, and on the entire data using Mann Whitney U test. To show continuity in the position of the section the stem was measured at its widest part from all the sections, Figure 7.14.

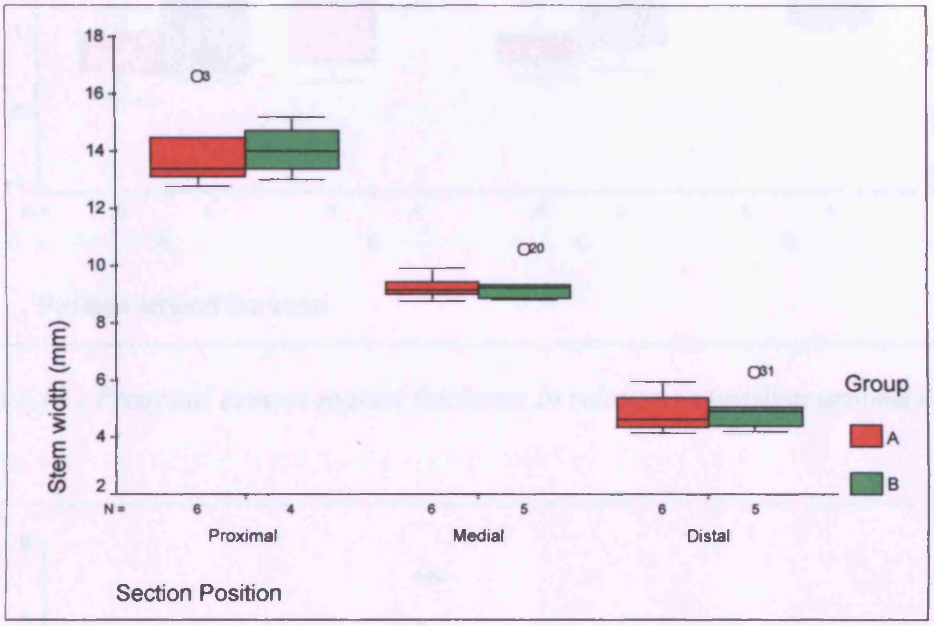

Figure 7.14 - Width of stem measured from each histology section

There was no significance in the average medial and proximal cement mantel thickness when comparing all the data and the paired data. There was also no difference between the positions round the stem medially or proximally using the paired data. However, using the non-paired data position D (lateral) highlighted a difference between the two groups proximally (Figure 7.15), this was not observed medially (Figure 7.16). Comparison of both groups found no difference between the proximal and medial cement mantel thicknesses.

Twenty-four cement thickness measurements were taken from the distal sections containing cement, there was no significant difference in thickness between groups. Very little penetration of the cement into the graft was observed for the three positions in either group. Consequently no attempt was made to measure this variable.

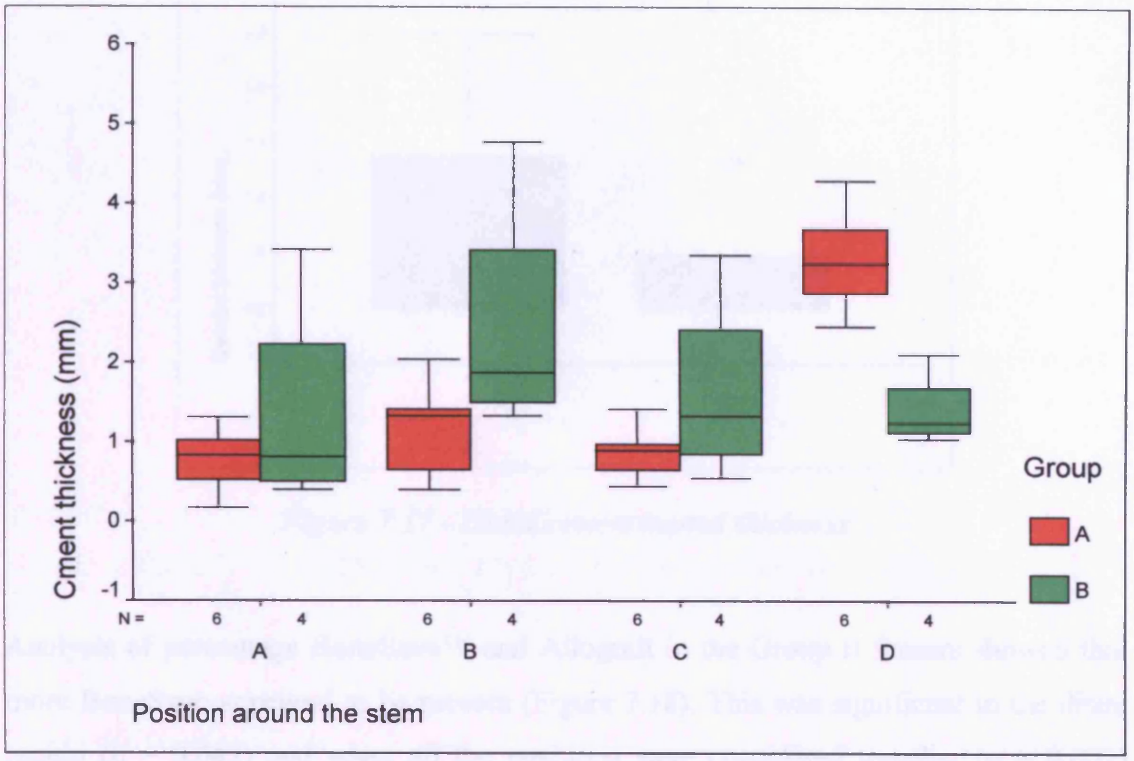

Figure 7.15 - Proximal cement mantel thickness in relation to position around the stem

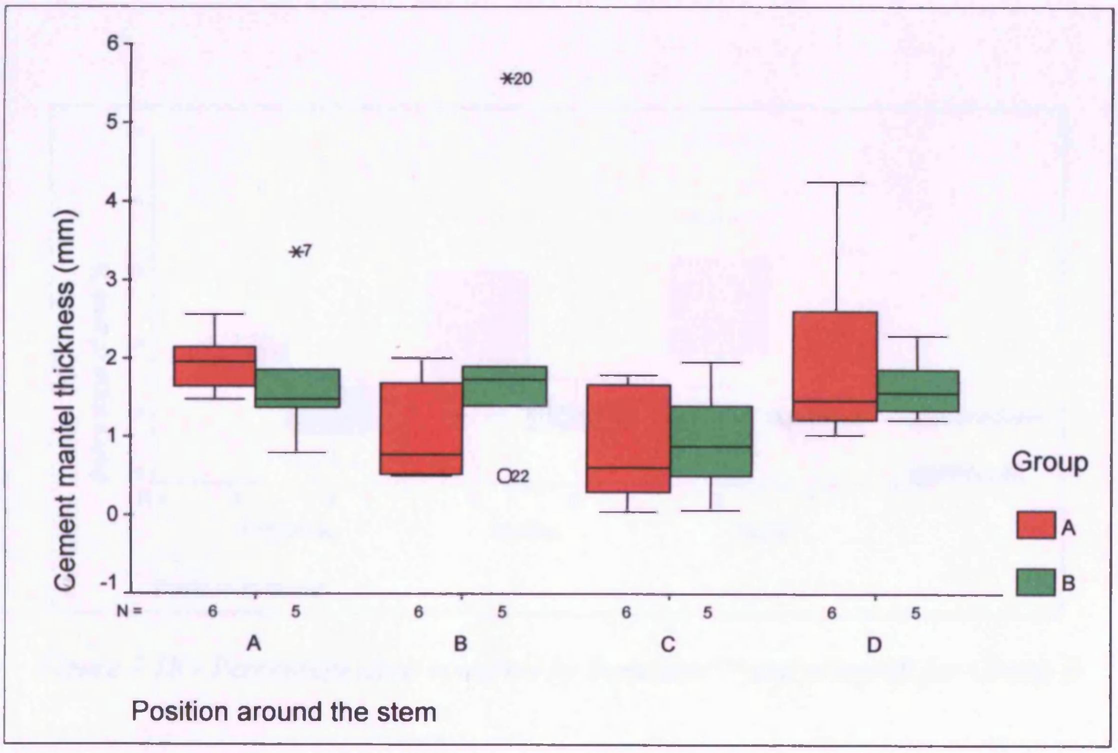

Figure 7.16 - Medial cement mantel thickness in relation to position around the stem

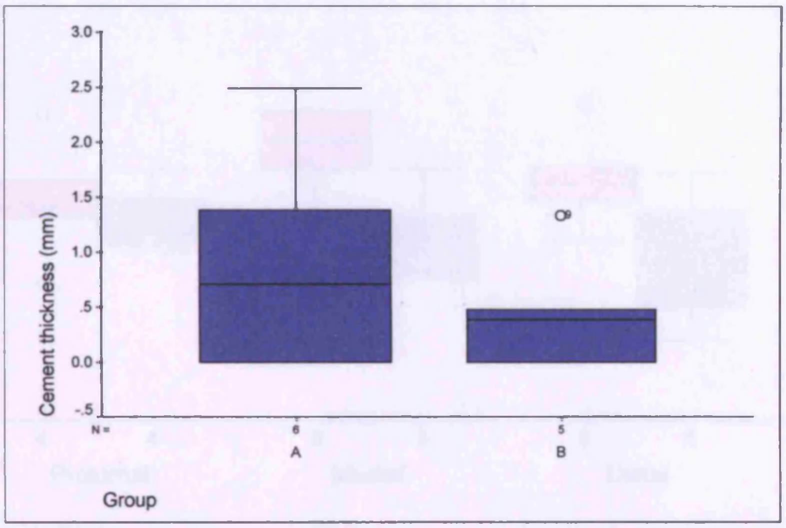

Figure 7.17 - Distal cement mantel thickness

Analysis of percentage BoneSave™ and Allograft in the Group B femurs showed that more BoneSave appeared to be present (Figure 7.18). This was significant in the distal region ($p = 0.043$) and when all the positions were considered together ($p = 0.002$) (Wilcoxon paired tests). The average ratio ± SD of BoneSave™ to allograft was 1.64 ± 0.52. The porosity values in the paired femurs were similar (Figure 7.19).

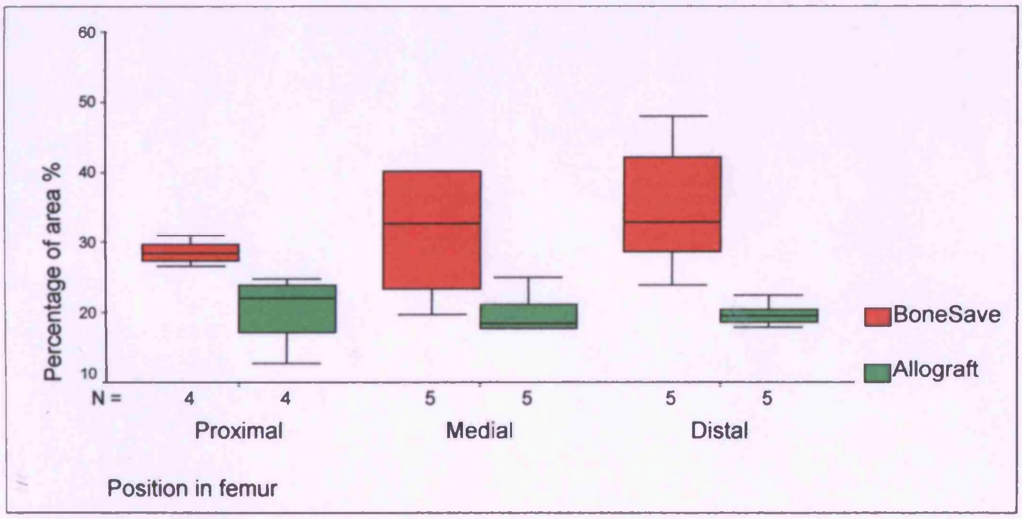

Figure 7.18 - Percentage area occupied by BoneSave™ and allograft for Group B

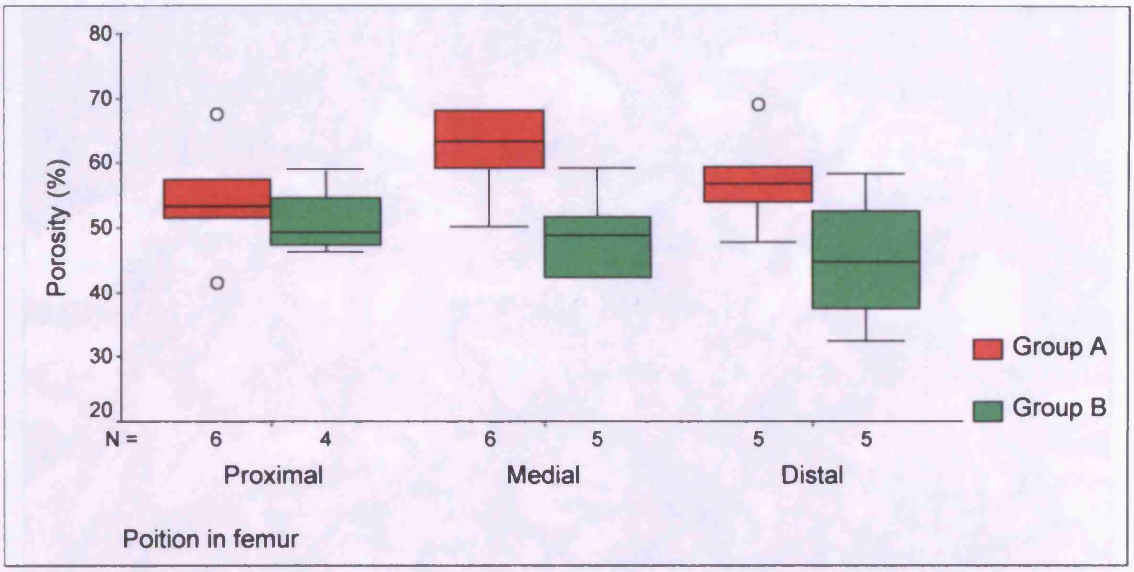

Figure 7.19 - Porosity of femurs at different positions down the femur

Figure 7.20 and Figure 7.21 are examples of the micro sections at times 20 magnification. Both the cement and host bone are visible in these pictures on either side of the graft.

Figure 7.20 - Micro section of allograft specimen (magnification x 20)

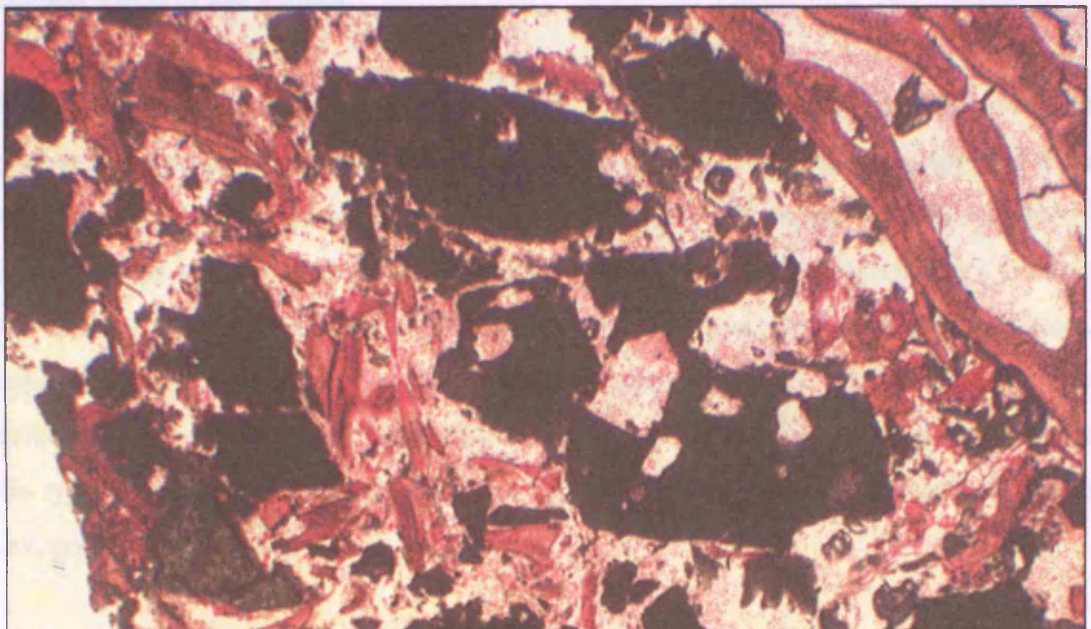

Figure 7.21 – Micro section of BoneSave™ / allograft sample (magnification x 20), BoneSave™ shows up black

7.4 Discussion

The purpose of this study was to evaluate the mechanical performance of allograft extended with BoneSave™ at time zero, in a realistic femoral impaction grafting model, with pure allograft as a control. Consistency of the impaction technique was measured using the modified slap hammer described in Chapters 3 and 4. The results from the hammer found that there was no significant difference in the average forces or sum of forces between the two groups. This implies that the superior mechanical results in the BoneSave™ were not created by the surgical procedure. However there were differences in the forces between the pairs of femurs, particularly Femurs 1 compared to the others. This may have been caused by the size of the femur or simply how the surgeon impacted on the day. This may affect the mechanical results in either a positive or negative way; if the force varied because a greater quantity of graft was required, it is possible that a greater amount of subsidence would be expected. However, if there was no apparent reason for the excess forces these stems may be more stable. The variation of average forces and sum of forces appears to be reasonably consistent between left and right pairs of femurs, which would tend to indicate that the variations were due to size and shape of the femurs.

The mechanical testing was performed in a hydraulic loading machine with the specimens mounted in the anatomical position. A flat plate was used to apply the force, with the intention that it would allow for any horizontal shift in the head. However, this did not always work. Consequently the femurs would have been subjected to a different type of bending than was intended. The mechanical test was run at 6 Hz, which is much higher than in-vivo. Bone is visco-elastic, consequentially the reduction in recovery period between loading may have resulted in increased fatigue. Another limitation to this type of testing is that it ignores the support of the femur in-vivo offered by the surrounding muscles and soft tissue.

The initial bone mineral density, measured with dexa scans, did not show any correlation with bone fractures during surgery or mechanical testing. However this did not take into account any variations in rasping the bones, which may have influenced results.

The cadaveric femurs had been frozen and fixed in formal saline. Although freezing the bone should not have major impact on the mechanical properties (Boyce et al, 1999), the fixing process may have affected their stiffness. Work by Currey et al (1995) found that with bovine bone fixing in formal saline resulted in a large reduction in impact energy absorption, but only minor changes in Young's modulus.

The femurs, and therefore the stem sizes used, varied between pairs. It would be difficult to remove this inconsistency using cadaveric femurs. However using a composite femur model such as Sawbones (Pacific Research) would remove this variable. Sectioning of the femurs showed that there were no major differences in the cement mantel between the two groups, which could have affected the stability of the implant. The sections also showed that once impacted the ratio of BoneSave™ to allograft was actually higher than the anticipated 1 : 1 and was actually 1.64 : 1. It had been hypothesised that the graft would be impacted more distally than proximally, due to the nature of the surgical technique and compaction during loading. However the microsection results found that the porosity was similar for both graft types and did not alter significantly with position down the femur. This indicates that the surgeon was able to impact evenly, and any consolidation of the graft during loading did not have a significant effect on the porosity.

7.5 Conclusion

This study has shown that samples that have had femoral impaction grafting performed using allograft which has been extended with 50% BoneSave™ will have superior initial stability than using allograft alone. The modified slap hammer showed that although there were no significant differences in the surgeon's impaction technique when using the BoneSave™ / allograft mix compared with just allograft, his technique did vary between different sets of femurs.

Chapter 8

Mechanical Testing of ApaPore-60 as a Bone Graft Extender in Sawbones

8.1 Introduction

ApaPore-60 is a synthetic bone graft extender that ApaTech Ltd[1] are hoping to bring to market in the foreseeable future. Bone graft extenders are desirable in impaction grafting because there is a shortage of Allograft available. ApaPore-60 is a 60 % porous sintered pure hydroxyapatite granular substance that is produced in two sizes, 2 - 4 and 5 - 10 mm. It is a stochiometric material having a calcium to phospate ratio of 1.67. In Chapter 7 a similar product, BoneSave™, was mechanically tested in fomalin fixed cadaveric bones to assess its initial stability when mixed with Allograft. BoneSave™ was also tested mechanically in tubes designed to mimic the set up of an ovine model (Blom et al, 2002). The aims of this Chapter are similar to the aims of the study described in Chapter 7: to investigate the use of ApaPore-60 as a bone graft extender, particularly in the application of femoral impaction grafting. However in this study Sawbones are used to replicate the femur, rather than cadaveric bones. Cadaveric bones are difficult to obtain, they vary in size and mechanical stiffness. Their mechanical properties are also affected by the fixing technique and any drying out that occurs during testing. Subsequently, second generation Sawbones[2] were chosen for their availability and uniformity of size and mechanical properties. These Sawbones are proven to behave similarly to real femurs (Cristofolini et al, 1996) and have a E = 18.6 Gpa in tension and, E = 14.2G Pa in compression. Two groups of six Sawbones were impacted with graft and had Exeter stems cemented into them. In Group A Allograft was used, in Group M a 50:50 mix by volume of Allograft and ApaPore-60 was used. The Sawbones were then mounted into a hydraulic loading machine and subjected to 25,000 loading cycles. Movement of the stems was measured.

Hypothesis – The inclusion of ApaPore-60 with Allograft will reduce the subsidence observed during the mechanical test.

This study was conducted with the help of James Pegrum as part of his BSc in Orthopaedics.

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[1] ApaTech Limited, Queen Mary, University of London, Mile End Road, London, E1 4NS

[2] Sawbones Europe AB, Krossverksgatan 3, 216 16 Malmö, Sweden

8.2 Methodology

Twelve Sawbones were used in this study, six in Group A (Allograft), and six in Group M (Allograft / ApaPore-60 Mix). Each group was investigated in batches of three, and the selection of each Group was alternated between batches.

8.2a Preparing of the graft.

The Allograft was prepared in a Noviomagus Bone Mill[1] from twenty human femoral heads, which had first had the cartilage and any soft tissue removed with a scalpel. (The femoral heads were collected at the Whittington Hospital, London, and Southmead Hospital, Bristol, with patient consent.) Two sizes of rasps were used, medium and large. Ninety percent of the Allograft was prepared with the medium rasp, whilst the remainder was produced with the large rasp. The two graft sizes were prepared to mimic the surgical procedure of the Exeter Group (Gie, personal communication). All the graft was prepared in advance and in order to minimise variations each size was fully mixed before being frozen in small batches.

Prior to impaction the required quantities of pre-morsellised graft were fully defrosted and then washed in warm tap water for 10 minutes and patted dry. For Group A femurs the graft was then ready for use. In the Group M equal volumes of washed Allograft were mixed with blood soaked ApaPore-60 (Figure 8.1). Approximately 1 ml of fresh human blood was required for each 5 grams of ApaPore-60. The 2 - 4 mm ApaPore-60 granules were mixed with the small Allograft, and 5 – 10 mm ApaPore-60 granules with the large Allograft. Masses and volumes were then recorded.

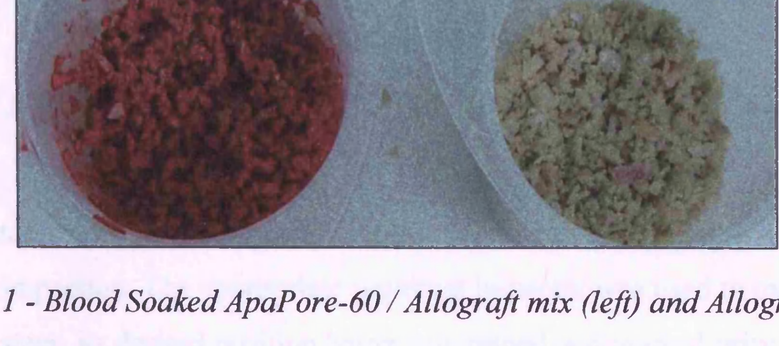

Figure 8.1 - Blood Soaked ApaPore-60 / Allograft mix (left) and Allograft (right)

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[1] Spierings Medisch Technieck

8.2b Preparing of the Sawbones.

Twelve large left Sawbones were used in this study. A template was created and each Sawbone marked for the removal of the femoral head and position of the distal plug. The femoral heads were cut off using a band saw. The foam was rasped out from each of the Sawbones to the marked position of the distal plug, leaving the fibreglass cortical shell.

8.2c Surgical Procedure.

The surgical procedure was intended to mimic as closely as possible that of live surgery, as described in the Introduction (Chapter 1). The Exeter X-change revision instruments were used with the addition of the modified slap hammer, which can record the impaction forces as described in Chapters 3 and 4. Extensive research, using the slap hammer was undertaken in order to quantify the impaction technique of several surgeons (Chapter 4). The operative procedure was conducted in the light of discussion with the surgeons and observations of their technique.

The Sawbone was clamped in a vice and a 12mm distal plug inserted to position 20 mm distal from the anticipated position of the tip of the stem. A metal washer was placed inside the plug, in order to visualise it on an x-ray (Figure 8.2).

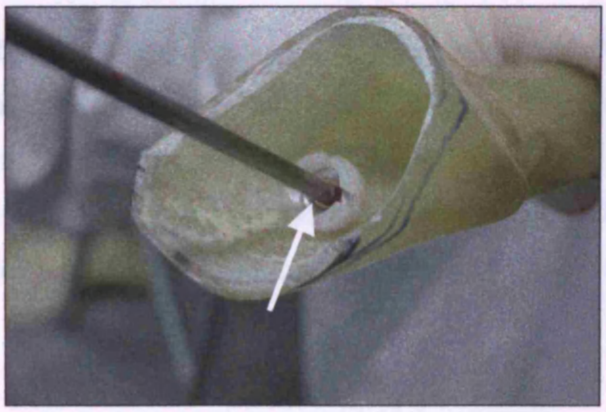

Figure 8.2 - Distal plug with a metal washer being introduced into the Sawbone

Distal impactors were inserted into the hollow Sawbones and their position marked to prevent over impaction. The appropriate proximal impactor was used to match the No. 1 sized Exeter stem, its desired position being determined and marked prior to the start of impaction. The No. 1 sized Exeter stem (44 mm offset) was chosen to allow for the largest possible graft mantel. The graft was added to the Sawbone in batches using a cut off 20 ml syringe so that weight and volumes could be recorded. Each batch of graft was impacted with the appropriate distal or proximal impactor and the forces recorded using the modified Exeter slap hammer described in Chapter 3 of this thesis. Following the Exeter technique (Gie, personal communication), medium sized graft was used to fill approximately three quarters of the Sawbone, after which the large graft was used to fill the remainder. Once the Sawbone was filled with graft and the proximal impactor had been driven to the correct position, the hand held impactors were used to compress a top layer of graft around the proximal impactor. Figure 8.3 shows proximal impaction of Allograft in a Sawbone

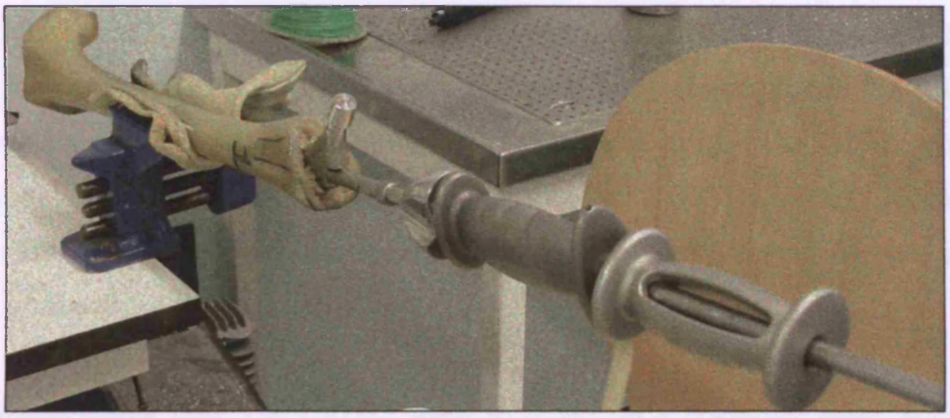

Figure 8.3 - Impaction of Allograft into a Sawbone

Once the graft was fully impacted the proximal impactor was carefully removed and the stem cemented into the cavity. The cement was mixed under vacuum and injected into the hole using a cement gun (Figure 8.4). The stem was then pushed into the cement to the marked position. A small amount of cement was used to cover the top of the graft, however care was taken to keep this layer as thin as possible to prevent it affecting the mechanical stiffness.

Figure 8.4 - Inserting the cement into a Sawbone containing Allograft/ApaPore-60 mix

8.2d LVDTs.

Linear variable differential transformers (LVDTs) with a 10 mm travel were used to measure micro motion and subsidence between the stem and the Sawbone, type WA/10mm[1]. The LVDTs come in two parts, one of which slots inside the other. Each part must then be firmly mounted onto the desired reference points, between which the displacement values are to be measured. To measure the subsidence and micro motion of the prosthesis into the Sawbone, pairs of LVDTs were mounted posteriorly and anteriorly on each specimen. The larger part of each LVDT was mounted on a circular clamp, which was fixed to the Sawbone using three pointed bolts. The other half was mounted to the top of the stem through a specially drilled and tapped hole. Care was taken to attach the lighter half of the LVDTs to the prosthesis so that the additional weight did not affect its movement. Both parts of the LVDTs were mounted through swivel joints to protect the LVDTs from unexpected movement. Figure 8.5 illustrates the mounting of the LVDTs. Due to the offset in the mounting of the LVDTs, posterior rotation of the stem induces a reduction in the posterior LVDT reading and increases the anterior LVDT reading. Subsequently the two readings were added together and divided by two to cancel out this effect.

The measurements from the LVDTs were recorded on a computer using a program called Catman® Express[1]. To test three sawbones at once six LVDTs were used simultaneously, connected via an amplifier (Spider 8)[1] to the computer. Using Catman® Express, the six LVDTs were programmed in and scaled to translate their milli-volts into milli-meters. The testing was recorded using periodic measurements with two graphs. The upper showing the overall recording and the lower, real time display. The data was then recorded and transferred into Microsoft Excel and analysed.

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[1] HBM United Kingdom Ltd., 1 Churchill Court, 58 Station Road, North Harrow, HA2 7SA

8.2e Mechanical testing

The mechanical test was performed in the Red Rocket, a six station hydraulic loading machine. The Sawbones were loaded in the anatomical position of 7 degrees valgus and 9 degrees posteriorly. With only three specimens being tested together, the unused loading stations were blanked off. The Sawbones were positioned in pots on their two condyles, to give the natural 7 degrees valgus, with the prosthesis head directly above the condyles. Low melting point alloy was poured into the pot and allowed to cool and set. Low melting point alloy is liquid above 74 degrees centigrade; this was heated in a special water bath. To obtain the posterior rotation the pots were fixed to the table via a 9 degree wedge.

The load was applied to the prosthesis head by a spherical piece of acetal mounted onto a ball bearing plate, which allowed for horizontal travel (Figure 8.5). Sinusoidal loading at 2 Hz was applied under the following loads: 600 N, 1 kN, 1.4 kN, 1.8 kN and 2.2 kN, each loading step lasting for 5000 cycles. A lower load of 400 N was used for all steps. Between each loading step, a pause of fifteen minutes was taken to allow relaxation: During these periods very light contact was maintained on the prosthesis to prevent the bearings from falling off. The Red Rocket was calibrated prior to testing using a load cell (U2000 5KN[1]) with a conditioning amplifier[2] mounted under one actuator and with the remaining five blanked off. Calibration was performed at all three loading stations used.

Vertical displacement of the prosthesis head was measured using digital height callipers at the beginning and end of each loading step (Figure 8.5). Radiographs were taken in the medial/lateral and posterior/anterior plane before and after mechanical testing. These were taken whilst the Sawbones were mounted in the pots to maintain continuity in their position. Arial photographs were taken of the Sawbones in the pots before and after loading. Measurements of the radiographs were undertaken to assess the displacement and rotation of the stem, and subsidence of the distal plug.

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[1] Maywood instruments, 17 Stadium Way, Reading, RG30 6BX

[2] RDP HowdenRDP Howden Ltd. PO Box 2677, Southam, CV47 0ZD

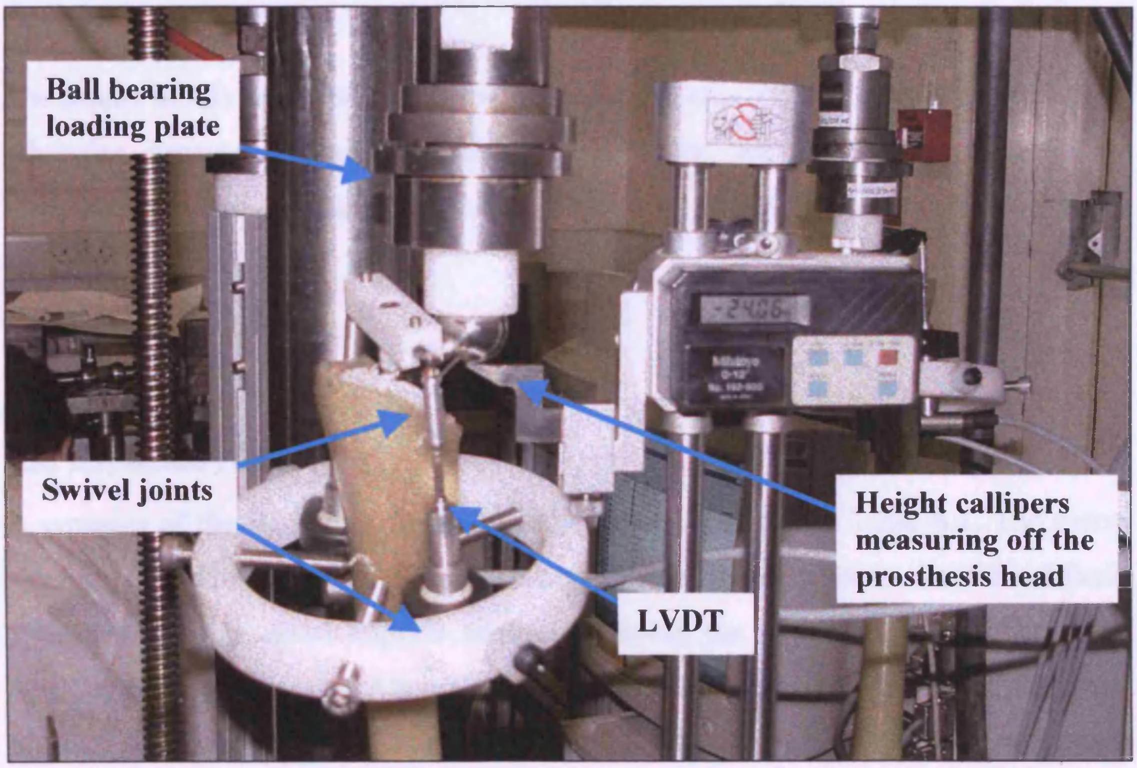


Figure 8.5 - Sample mounted in the Red Rocket loading machine

8.2f Sectioning the Sawbones.

Once the mechanical study had been performed, the Sawbones were fixed in formal saline and embedded in hard grade resin. Three histological sections, ~100 μm thick, were cut from each of the Sawbones, at proximal, medial and distal positions. The proximal section was cut just above the lesser trochanter and the medial section 50 mm below that. Both of these sections were cut transversely through the femur. The distal section was cut longitudinally through the centre of the Sawbone, over a 70 mm length above the plug. These sections were stained with paragon and analysed by light microscopy. The Cement Mantle Thickness was measured as the distance between the stem and where it first contacted the graft. Forty eight measurements around the stem were taken and averaged. A further 48 measurements overlapping the first were taken from the stem to the furthest position of the cement into the graft. These were averaged to give the Total Cement Thickness. The first measurement was taken from the Total Cement Thickness to give the Cement Penetration. The percentage of Bone and ApaPore-60 was calculated using the line intersect method. The porosity of the samples was taken as that not containing Bone or ApaPore-60, although it may have contained blood or other particles.

8.3 Results

The results in this study have been analysed using Mann Whitney U tests, unless stated otherwise, because the sample sizes were small (six) and the Sawbones used were independent. The significance level was set at $p \leq 0.05$. Averages are written ± standard deviation.

8.3a Impaction Forces

A synopsis of the impaction forces used in surgery is shown in Table 8.1. The forces were not, however, recorded during the impaction of femur 5 due to a technical fault. Significantly more distal impacts were used during the impaction of the Allograft / ApaPore-60 mix than with Allograft alone ($p = 0.028$). However the sum of the distal impacts and average distal impaction force did not show a significant difference between the two graft types. No differences were found when looking at the proximal impacts or all impacts grouped together. The average distal impaction force measured in the hammer in this study was 14.5 kN and the average proximal force was 17.5kN. These are comparable with those measured in surgery (Range average Distal Impaction Force 8.1 - 21.8 kN, Range average Proximal Impaction Force range 6.1 - 28.9 kN). Figure 8.6 illustrates the distal and proximal impaction forces of Groups A and B and compares them with those measured in live surgery in Chapter 4.

	Allograft						ApaPore-60 & Allograft Mix					
Femur No.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
No. of distal impacts	30	37	34	39		24	45	58	41	66	31	43
Average distal impact force (kN)	13.5	14.5	10.6	17.8		16.6	13.1	13.8	15.0	14.7	16.6	13.0
No. of proximal impacts	66	96	65	74		95	113	77	92	75	65	57
Average prox. impact force (kN)	18.8	13.8	18.9	17.4		21.7	14.8	15.9	15.3	13.3	22.9	19.9

Table 8.1 - Force measurements.

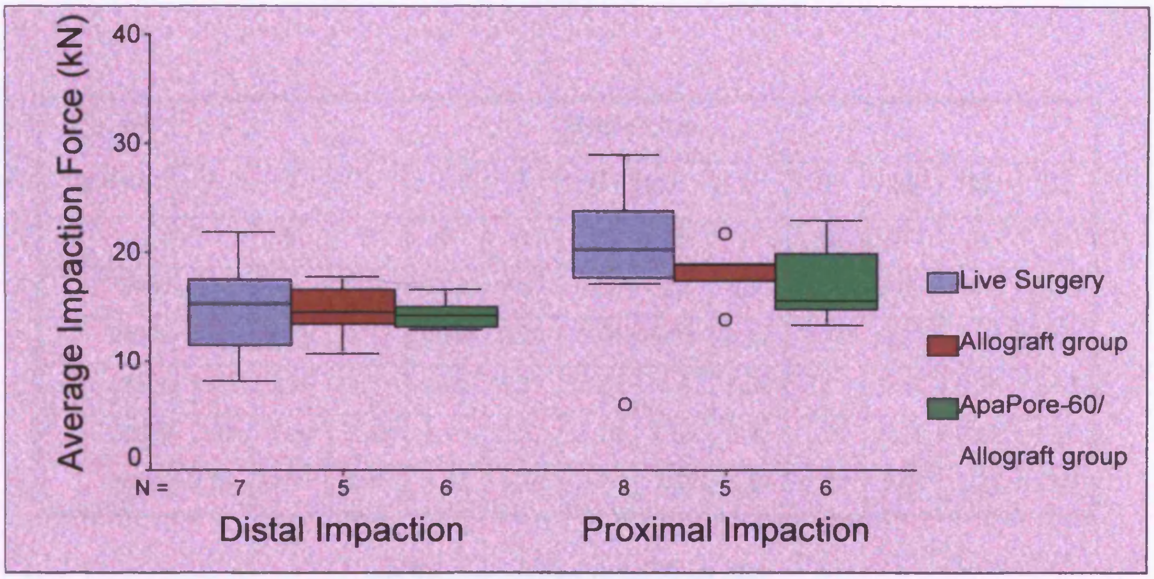


Figure 8.6 - Average impaction forces compared with those measured in live surgery

8.3b Graft quantities

The average volume of graft used in the Allograft group and the mixed group was 88.3 ml and 93.3ml, with respective average masses of 66.8 grams and 71.6 grams. No significant differences were found between the two groups. The volume inside the femur minus the proximal impactor volume was approximately 63 ml, indicating that the graft was compressed to roughly two thirds of its original volume.

8.3c Prosthesis Head Height

Figure 8.7 illustrates the migration of the head measured with the digital height calipers. This drop in the head height is a result of subsidence and rotation in all the planes of the prosthesis. After the first and second loading steps, no difference was found in the overall displacement of the prosthesis head in the Allograft group compared with ApaPore-60 / Allograft group. A significant difference was found after the third, fourth and final loading steps ($p = 0.025$, $p = 0.004$ and $p = 0.01$). Total average head movement Allograft group: 3.5 ± 0.7 mm and Mixed group: 1.8 ± 0.7 mm (Table 8.2).

No. of	Femur no.											
cycles	1	2	3	4	5	6	7	8	9	10	11	12
0	0	0	0	0	0	0	0	0	0	0	0	0
5000	0.35	0.85	0.34	0.11	0.09	0.26	0.6	-0.01	0.26	0.03	0.1	0.23
10000	0.56	1.16	0.72	0.86	0.74	0.58	0.98	0.22	0.49	0.33	0.25	0.62
15000	1.26	2.28	1.54	1.26	1.37	1.23	1.4	0.59	1	0.52	0.56	1.07
20000	2.03	3.29	3.39	1.75	2.22	1.75	1.62	0.83	1.21	0.75	0.68	1.38
25000	2.97	4.01	4.47	2.42	3.26	3.73	2.68	1.47	2.52	1.02	1.21	1.95

Table 8.2 - Head heights in mm

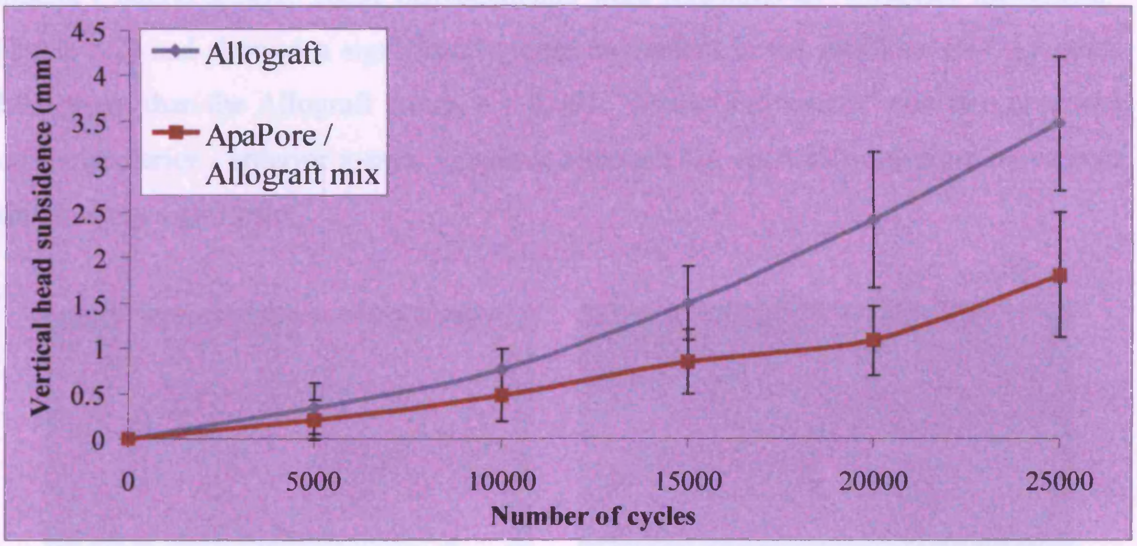


Figure 8.7 - Migration of the of prosthesis head measured using digital height callipers

8.3d LVDT data

The total average subsidence measured with the LVDTs was 0.29 ± 0.30 mm in the Allograft group and 0.12 ± 0.09 mm in the ApaPore-60/Allograft Mix group. The micro motion measured during the final loading phase was 0.20 ± 0.03 mm for Group A and 0.02 ± 0.07 mm for Group M. No significant differences in subsidence or micro motion were found between Groups A and M. The micro motion at the beginning and end of each phase was compared and showed no difference.

8.3e Radiograph measurements

Subsidence of the distal plug and the prosthesis tip in relation to the plug were measured on the medial x-rays, (Table 8.2). The prosthesis tip movement was greater in Group A than in Group M, however this was not significant ($p \geq 0.05$). In only one case in each group did the plug migrate, and only by 1 mm, which indicates that the plugs were firmly positioned.

Rotation of the prosthesis head about the stem's central axis was visible after loading and can be observed in the pre and post loading aerial photographs, Figure 8.8. This rotation was also observed by a sideways displacement of the prosthesis head in the medial / lateral x-rays. These displacements were measured as "posterior movement" (Table 8.2) and showed a significantly more movement in the ApaPore–60 / Allograft Mix group than the Allograft group, $p = 0.003$. "Medial movement" was also observed on the posterior / anterior x-rays. However although Group A showed more movement this was not significant.

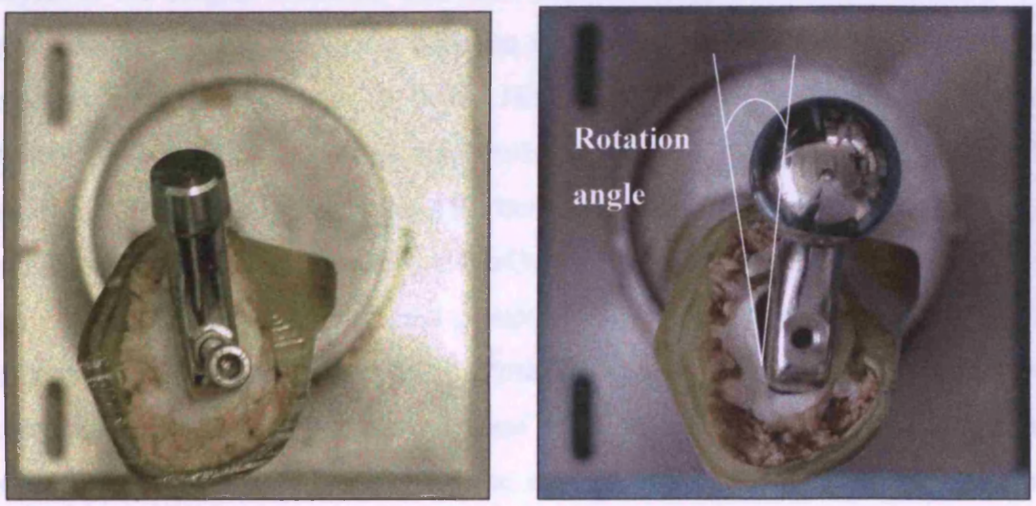


Figure 8.8 - Rotation of the prosthesis: Specimen 6 before loading (Left) and after loading (Right)

	Migration of stem tip (mm)		Migration of distal plug (mm)		Posterior movement of stem head (mm)		Medial movement of stem (mm)	
Group	**A**	**M**	**A**	**M**	**A**	**M**	**A**	**M**
	1	0.5	0	1	6.5	3.5	1	0.5
	0.5	0	1	0	10	5	0.5	1
	0	0	0	0	10	3	1	0
	0.5	0	0	0	6	1	0	0
	0	0	0	0	10	2	1	0.5
	1	0	0	0	10	3	0	0
Average±SD	*0.5±0.4*	*0.1±0.2*	*0.2±0.4*	*0.2±0.4*	*8.8±1.9*	*2.9±1.4*	*0.6±0.5*	*0.3±0.4*

Table 8.3 - Radiograph measurements

8.3f Histology Sections

Analysis of the cement found no difference in the Cement Mantle Thickness (average distance between stem and graft) between the groups, or within the groups between medial and proximal sections ($p>0.05$). However, in both the proximal and medial sections the Total Cement Thickness (average distance between stem and furthest distance into graft) was larger in the ApaPore-60/Allograft Mix group than the Allograft group; Proximal $p = 0.021$ Medial $p = 0.043$. The Cement Penetration values were only significantly different in the proximal group; $p = 0.043$. It was not unusual, with either graft group, to find that the cement had come into contact with the anterior cortical wall in proximal sections: This was also the case in the medial sections, plus it occasionally reached to other walls. A box plot of the cement mantle in the proximal sections is shown in Figure 8.9 and in the medial sections in Figure 8.10

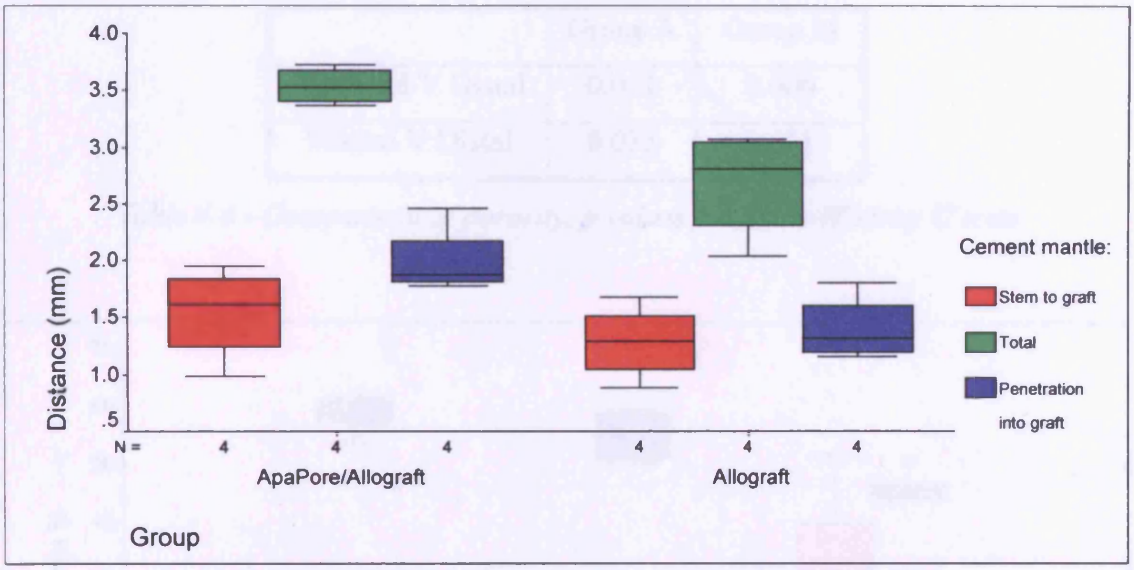


Figure 8.9 - Analysis of cement in proximal sections

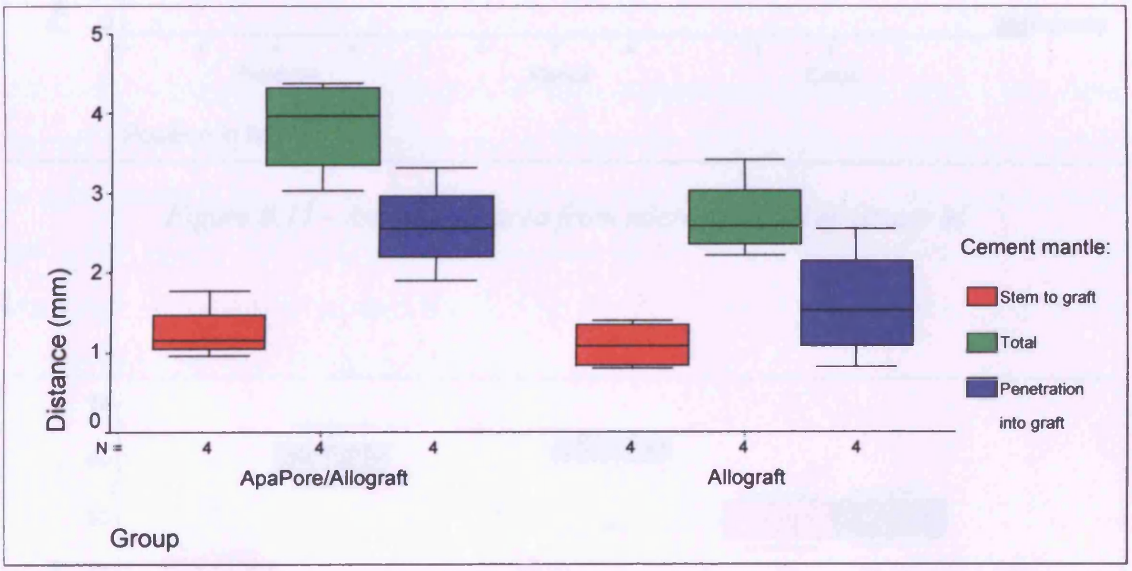


Figure 8.10 - Analysis of cement in medial sections

The micro sections found the ratio of ApaPore-60 to Bone was 1.22 ± 0.57 and was consistent irrespective of position down the femur (Kriskal wallis p>0.05). The porosity (area containing no bone or ApaPore-60) distally was significantly lower than proximal and medial in both groups (Table 8.4). A box plot of the percentage of ApaPore-60, allograft and porosity for the Sawbones in Group M is shown in Figure 8.11. Figure 8.12 is a box plot of allograft and porosity for the femurs in Group A. There was no significant difference in percentage porosity between the groups (Figure 8.13).

	Group A	Group M
Proximal V Distal	0.011	0.006
Medial V Distal	0.033	0.011

Table 8.4 - Comparison of porosity, p values for Mann Whitney U tests

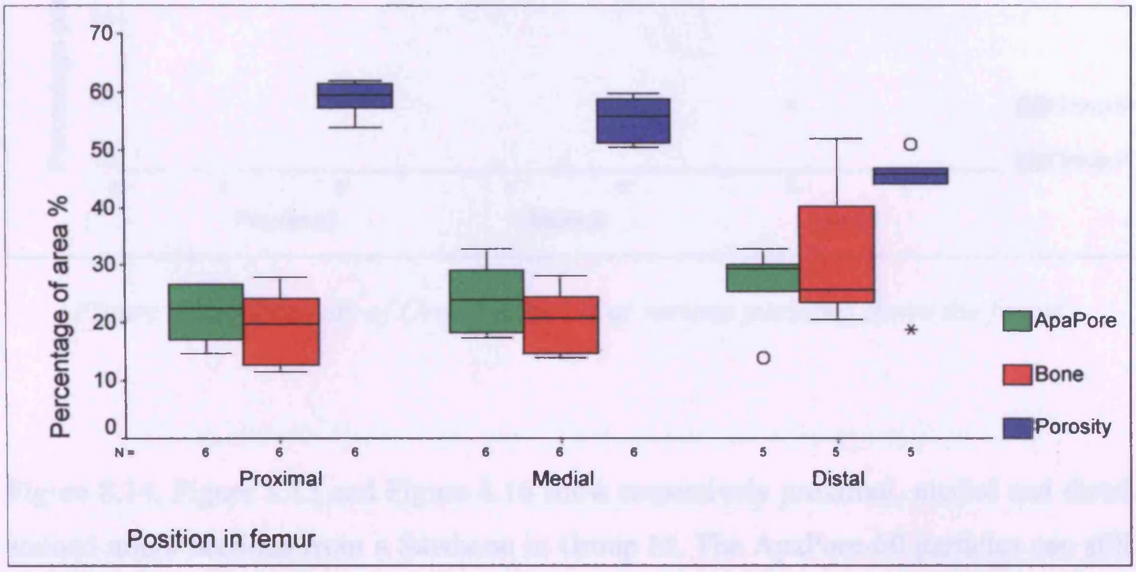


Figure 8.11 - Analysis of area from micro sections of Group M

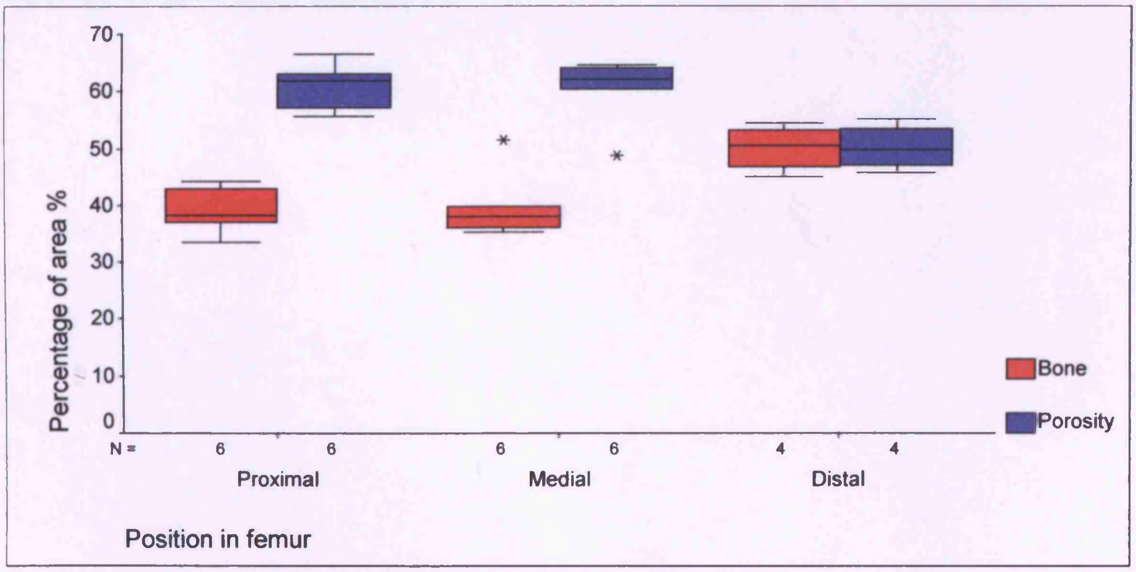


Figure 8.12 - Analysis of area from micro sections of Group A

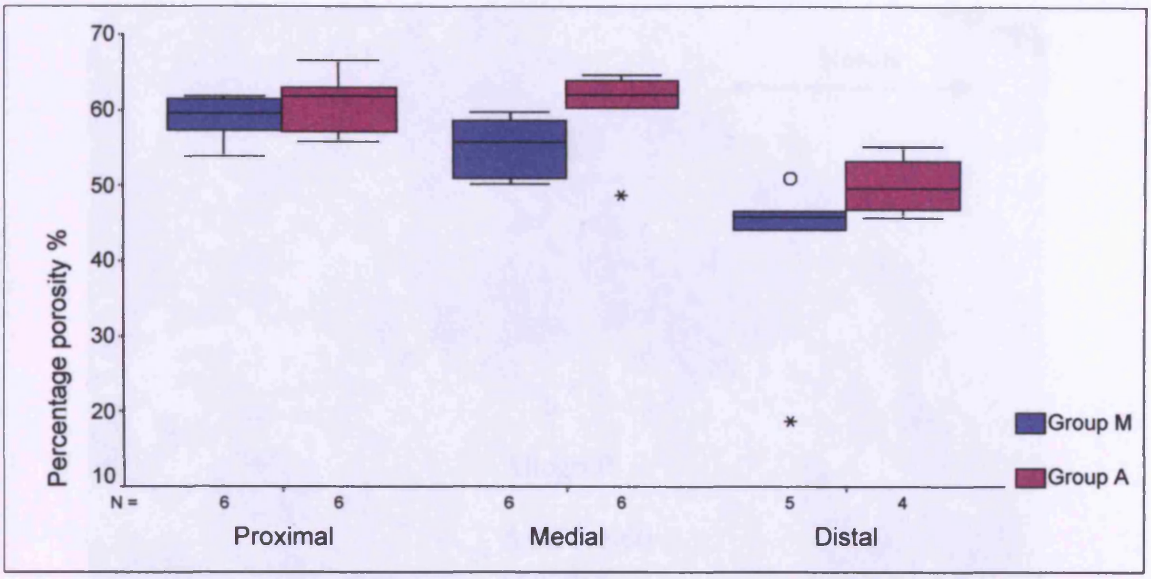


Figure 8.13 - Porosity of Group A and M at various positions down the femur

Figure 8.14, Figure 8.15 and Figure 8.16 show respectively proximal, medial and distal stained micro sections from a Sawbone in Group M. The ApaPore-60 particles can still be seen clearly in the proximal and medial sections. However in the distal section, there are areas where the ApaPore-60 and allograft have become very crushed. When examined under higher magnification, blood particles are visible in the pores of the ApaPore-60 granules (Figure 8.17).

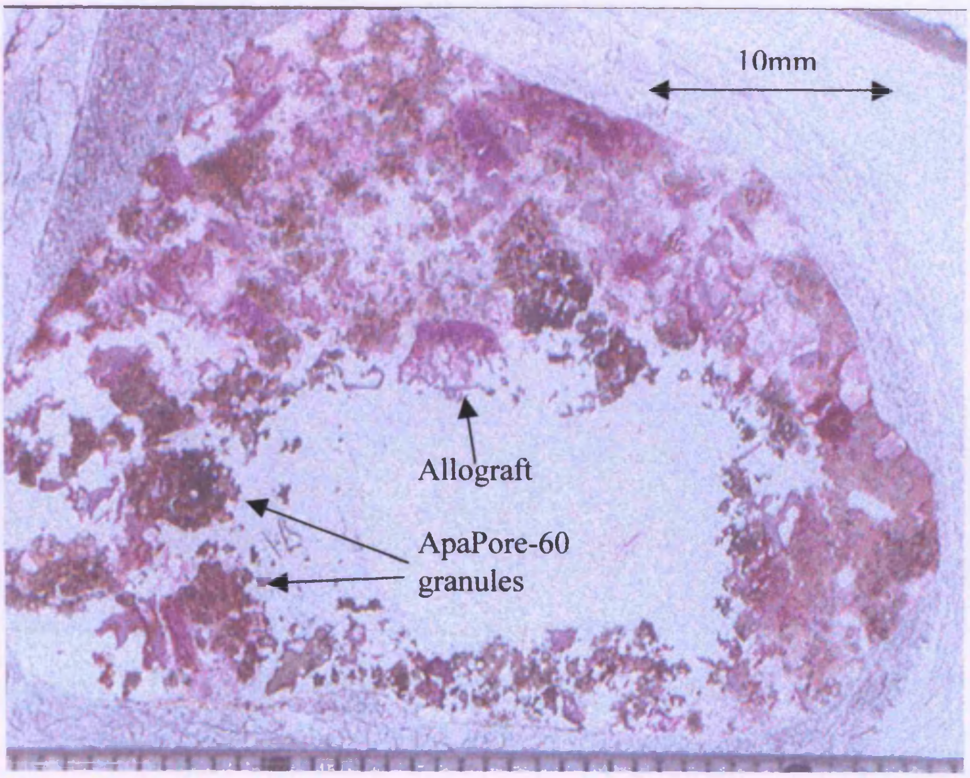


Figure 8.14 - Proximal section of Sawbone with ApaPore-60 / Allograft mix

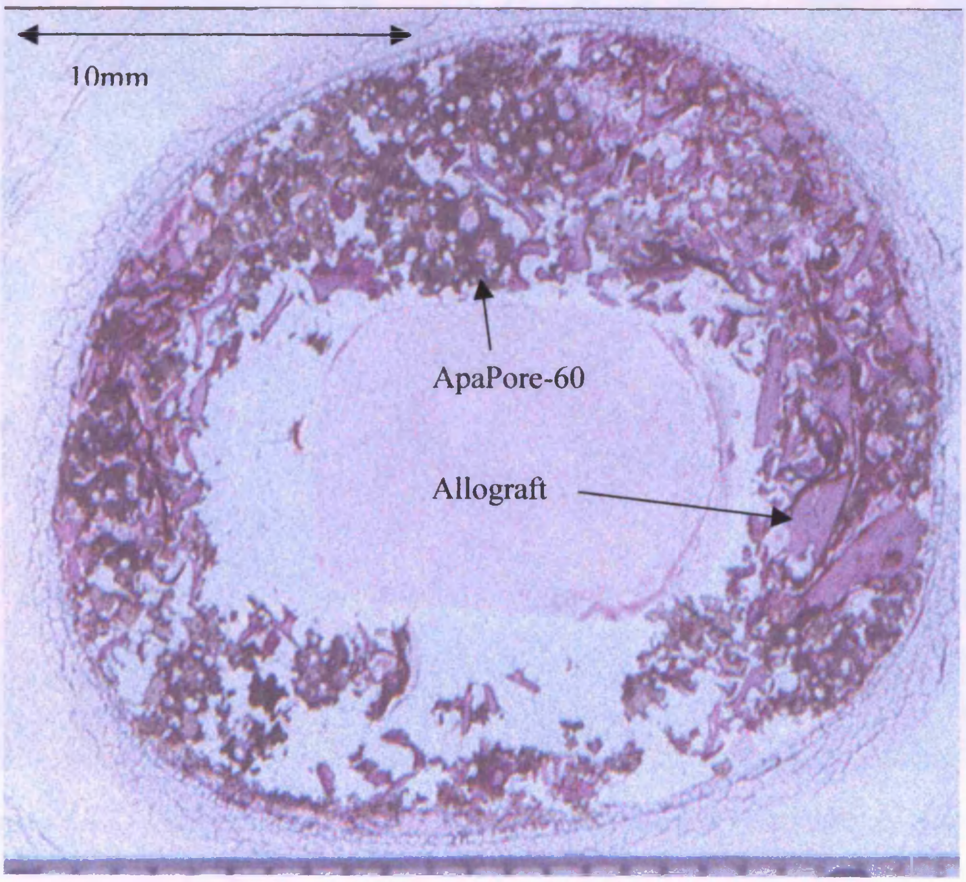


Figure 8.15 - Medial section of Sawbone with ApaPore-60 / Allograft mix

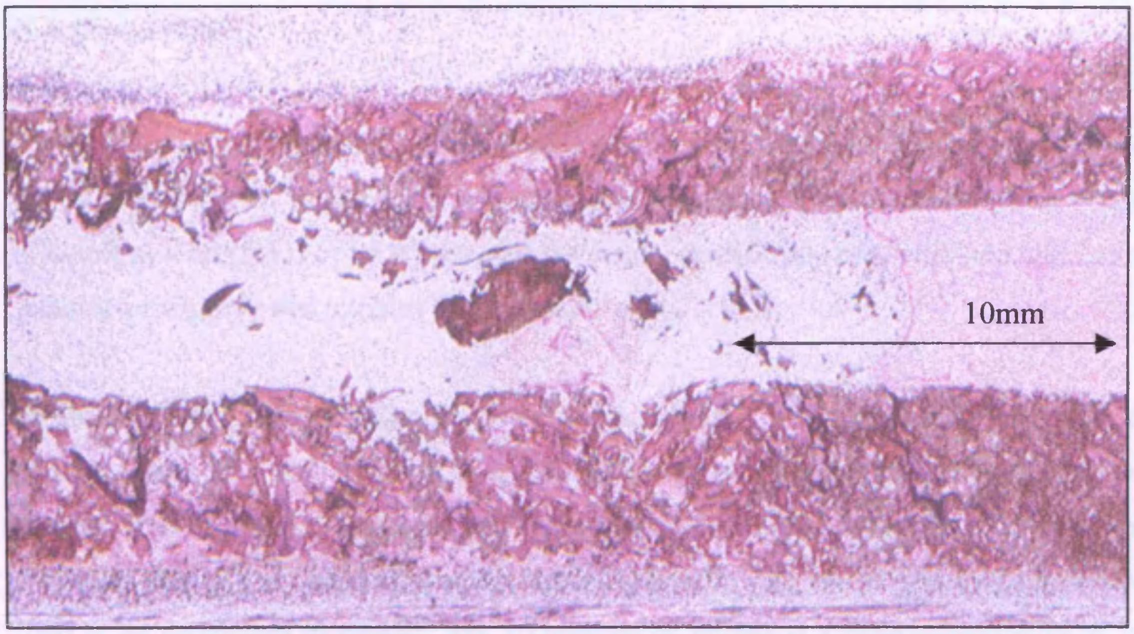


Figure 8.16 - Distal section of Sawbone with ApaPore-60 / Allograft mix

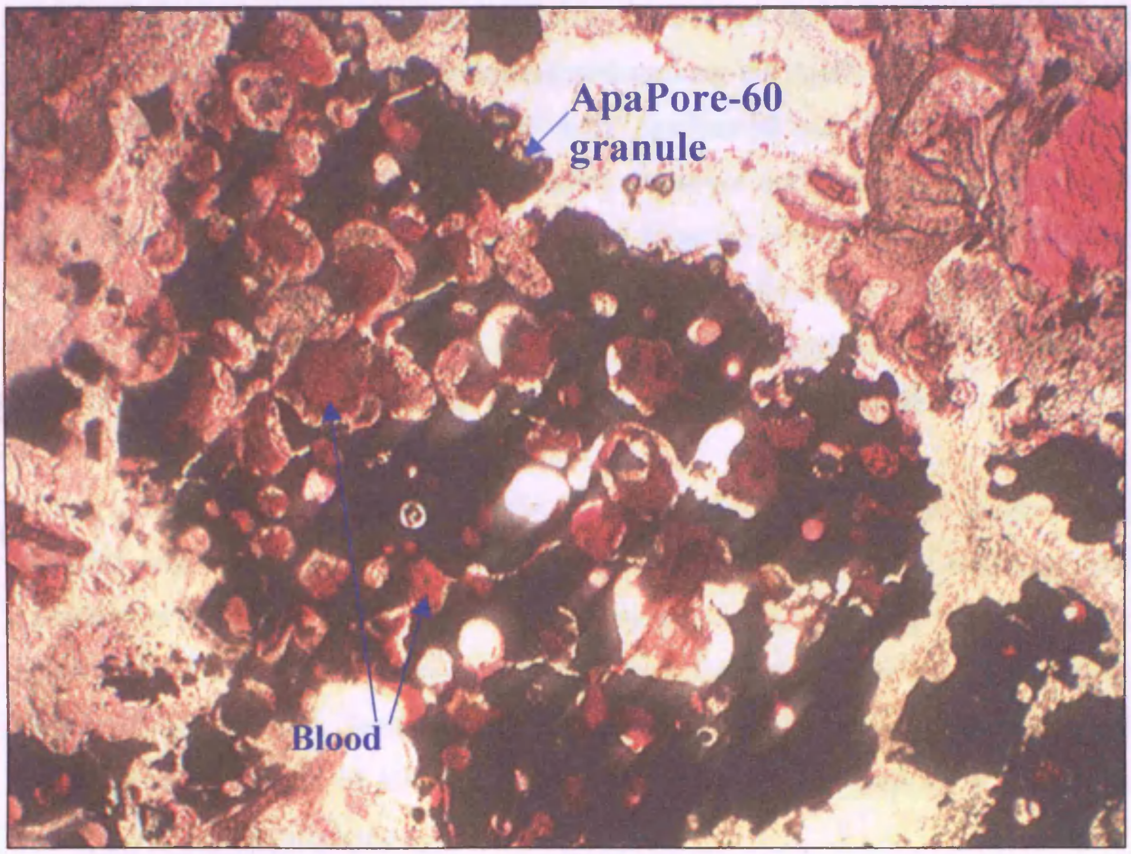


Figure 8.17 - Magnified view (x 10) of ApaPore-60 granule containing blood cells

8.4 Discussion

This project set out to investigate the stability effect at time zero of including ApaPore-60 as a 50/50 mix to allograft (Group M) in femoral impaction allografting, with allograft as a control (Group A). Overall the results showed that the combined mix gave reduced subsidence and rotation of the femoral stem.

In this study the Allograft was rinsed in warm water for 10 minutes to reduce the fat content. This does not remove as much of the fat as washing following the North London Tissue Bank procedure (NLTB) (see section **5.2a**), which was used in both ovine studies of this thesis (Chapters 5 & 6). However the NLTB protocol takes too long to be performed in surgery, but 10 minutes of rinsing is a good compromise as it still removes much of the fat, hence ApaTech intend to recommend such a procedure prior to mixing allograft with ApaPore-60 in live surgery.

ApaPore-60 does not have the same cohesive properties as allograft particles because it is dry and brittle. Hence ApaTech recommend soaking the ApaPore-60 in fresh blood from the patient, prior to its use. In this study ApaPore-60 was soaked in fresh blood and this did improve the cohesive properties. However during impaction, the mixed group behaved differently. When impacting the allograft, it was able to hold its shape during impaction with the proximal impactor, but the ApaPore-60 / Allograft mix had a tendency to collapse as soon as the proximal impactor was withdrawn: It could only maintain its shape once the graft was impacted to the top of the Sawbone.

It was intended that the surgical procedure would mimic that of live surgery. The modified slap hammer (Chapter 3) was able to show consistency in the technique, and also that the impaction forces were within the range of those currently used in surgery (Chapter 4). A significantly greater number of distal impactions were used in Group M compared with Group A. However since no difference was found in the average distal impaction force or sum of all distal impactions, this does not indicate a significant disparity between the impaction of the two groups.

The low movement of the distal plug indicated strong fixation, this was possibly because the Sawbones foam core was only removed to just below the desired position of the plug. However in a real femur, cancellous bone is only found at the end of the long bone, so this support would not be available. Despite being superior to the normal conditions, it produced a uniform plug fixation and hence removed another variable.

Subsidence of the prosthesis head, measured by the height callipers, gave larger readings than those of the LVDTs and x-rays. The head heights showed a significant difference between the groups, but the LVDT subsidence values and x-ray results did not. This disparity in results was caused by the rotation of the stem, in all planes, which added to the vertical movement of the head. This rotation was measured on the x-rays as posterior movement of the prosthesis head and was found to be significantly greater in Group M. It is common for subsidence of a stem during mechanical loading experiments to be measured directly from the machine's internal displacement reader, as was the case in the BoneSave™ cadaveric study (Chapter 5) and the study on BoneSave™ by Blom et al (2002). The Red Rocket does not have an internal displacement reader. However, a measurement of the prosthesis head heights by the callipers is an identical reading. This study therefore highlights the inaccuracy of such measurements, as it assumes that subsidence of the prosthesis head is equivalent to the subsidence of the prosthesis into the femur, when in fact it may be an accumulation of rotation and subsidence of the stem into the femur.

The measurements from the LVDTs should be comparable with the migration of the stem on the x-rays. Whilst the measurement of the x-ray is direct, the LVDTs have to be mounted with an offset, due to their physical limitations. Pairs of LVDTs were used to cancel out any variations caused by the posterior rotation of the stem. However medial and axial rotation of the prosthesis will also add to the displacement values of the LVDTs. Since the results show that the stems did move in both of these planes, x-ray measurements of stem displacement are more accurate.

This model did not take into account the support given to the bone by the surrounding muscles and soft tissue. Therefore the Sawbones experienced high bending which would not be expected in normal physiological loading conditions. However the subsidence observed was within the range that might be expected clinically, therefore the model is of relevance.

The micro sections were able to show that the porosity of the graft is unaffected by the inclusion off ApaPore-60, so should not affect the revascularisation rate. The sections also showed that the graft is more compacted distally than medially and proximally for both groups. This is likely to be an effect of the impactors. The distal impactors are rods with a bulbous end, whereas the proximal impactors are femoral stem shaped. Hence for a similar force a much higher pressure will act on the graft under distal impaction than proximal impaction. The penetration of the cement into the mixed graft was greater than into the allograft, although not significantly: This may have contributed to the superior stability of this graft type.

An in-vitro study is only capable at looking at the time zero mechanical stiffness. To understand the long term mechanical properties of ApaPore-60 an in-vivo study would need to be conduced.

8.5 Conclusion

This study produced a sound method for testing synthetic bone grafts at time zero. Multiple LVDTs would be required to obtain accurate subsidence measurements of the stem in such a model. Alternatively measurements could be taken directly from x-rays. Subsidence measurements from the prosthesis head are likely to be an addition of movement of the stem by migration and rotation in the femur. This study indicates that inclusion of ApaPore-60 to Allograft will offer better initial stability than Allograft alone during femoral impaction grafting. However further research needs to be undertaken to investigate the long-term feasibility of ApaPore-60.

Chapter 9

Overall Discussion and Conclusion

Femoral impaction grafting is a technique where bone graft is impacted into the femur prior to cementing a stem in place. The technique is designed to compensate for bone stock loss in revision surgery, however it has associated problems of implant movement / subsidence and periprosthetic fractures. The hypothesis for this thesis was that the stability and remodelling of impaction grafting could be improved, either by changing the graft size or by adding a synthetic graft.

In order to investigate the stability and remodelling the forces used to impact the graft clinically had first to be measured so that realistic laboratory based studies could be carried out. The first experimental chapter of my thesis investigated the forces used in surgery to impact the bone graft. Forces were measured following the adaptation of a surgical slap hammer. It was hypothesised that under-impaction of the graft may cause implant movement, whilst over impaction could cause tight packing resulting in a slower remodelling process. Before these concepts could be investigated it was necessary to measure the forces used during the surgical technique.

The modification of the Exeter hammer enabled almost real time measurements of impaction forces through out an entire operation. Through calibration it was realised that approximately two thirds of the measured force applied to the hammer was not being applied to the graft. Inertia of the hammer accounted for the loss of this force. The recommendations of such a finding are that the slap hammer (excluding the sliding mass) could be manufactured from a lighter material to reduce this effect. Although this may have also altered the overall force on the graft and changed the surgical conditions. The hammer was used to measure the forces in surgery and it was also used during two other laboratory experiments investigating synthetic bone graft extenders. When used in surgery the results showed that the technique did vary between operations and between surgeons. Also the technique of any given surgeon also varies for different patients. Consequently developing the slap hammer to produce a standard repeatable force did not appear to be the way forward. The study in the surgical forces was limited to nine cases measured from four different surgeons and follow-up periods of approximately a year. Consequently realistic conclusions on the appropriate surgical forces cannot be drawn from this aspect of the study. However it is intended that this work should continue with more measurements taken and the outcome of patients reviewed over a longer follow-up period. Nonetheless the surgical force readings were valuable because they formed the basis of the forces used during the in vivo and in vitro experiments, which allowed realistic graft properties to be investigated. In addition the hammer was used in Chapters 7 and 8 to measure the forces used to evaluate the technique used for two graft extenders and therefore gives a comparison with the results measured in surgery.

The mechanical and biological properties of the graft were investigated in relation to size, grading and the addition of granular Calcium Phosphate graft extenders. There has been much interest in the allograft's mechanical properties in relation to size, grading, and graft preparation. However work relating these factors to the biological properties of the graft is limited. Although the mechanical properties are essential for supporting the prosthesis when first inserted, if remodelling of the graft does occur this will offer much longer term support. In my thesis I investigated the effect of small, large and graded graft on mechanical properties and biological incorporation. The results showed that the graft type did not have an effect on the remodelling rate, which would contradict the views of Griffin et al (2001) who believe graded samples to be more advantageous. The Large graft had higher porosity and lower stiffness, in axial testing, than Small and Graded Groups. Tagil and Aspenberg (1998) found that impaction impairs osteoconduction, consequently it was anticipated that the Large graft might have superior biological results. However, this was not the case possibly due to the different nature of the two studies. The complicated grading of particle size did not show any significant advantages on the remodelling or axial stiffness, the use of small graft between 2 to 4 mm is therefore recommended from these findings.

The results of this graft size study also highlighted a significant decrease in bone mineral density after six weeks compared to twelve weeks post-operative. The density of bone can be directly related to mechanical strength (Augat et al 1998). This implies that during the early stages of remodelling the graft resorbs and mechanical stiffness decreases, but by twelve weeks more new bone is laid down and the mechanical stiffness increases. If this occurs clinically it could have important consequences that may lead to the graft becoming weak when the patient starts to mobilise.

Three of the projects in my study looked at Calcium Phosphate bone graft extenders, namely BoneSave™ and ApaPore-60. Bone graft extenders are currently being developed as bone graft supply struggles to keep up with the ever-increasing demand and ideally should improve the mechanical and biological properties of the graft. Ideally the development of these graft extenders will result in a total bone graft replacement, which would eliminate cross infection concerns and remove the complicated testing, storage and preparation of the graft and consequently reduce costs. In addition it would ideally provide more consistent patient outcomes.

The results of the graft sized project had shown a significant difference in bone mineral density between six and twelve weeks. So it was hypothesised that inclusion of a synthetic bone graft extender, BoneSave™, with allograft would reduce this drop in density observed after six weeks remodelling of allograft. Also that the drop in bone mineral density of allograft during remodelling would result in reduced mechanical stiffness. The stiffness of the remodelling graft was measured using a 10 mm square indenter in the centre of the graft site, with the surrounding cancellous bone tested to act as a control. Unfortunately the results did not find a significant difference in density or mechanical stiffness. This result was attributed to the different impaction force chosen for this part of my study, which was chosen to match the forces measured in surgery with the slap hammer. Unfortunately these data had not been available when the first study into bone graft size was conducted. Nevertheless this study did show that there was no disadvantage in terms of stability or remodelling if an artificial graft extender was used.

Following the use of a bone substitute material in an in vivo model the initial mechanical stability of BoneSave™ was investigated in cadaveric femurs, whilst a similar project was conducted on ApaPore-60, using Sawbones™ (glass fibre composite femurs) instead of femurs. The results of the BoneSave™ study were much more variable, undoubtedly the inconsistency of femur sizes contributed to this effect. In both of these projects the adapted slap hammer was used to measure the impaction technique so consistency for each graft type and with the allograft control could be observed. In the BoneSave™ study the inconsistency within the graft groups was possibly due to the size difference between femurs. The testing technique of the two projects was similar; the distal ends of the femurs were set in low melting point alloy and the prosthesis head subjected to cyclic loading. However in the BoneSave™ study a 6 Hz frequency was used and the force went up to 2 kN, and in the ApaPore-60 project the frequency was 2 Hz with a maximum load of 2.2 kN. Despite an obvious discrepancy in loading frequency, the load was similar so one would expect the control of allograft in each project to produce similar results. However the subsidence observed in the control of the BoneSave™ project was 2.31 ± 1.89 mm (after 10,000 cycles) and 3.5 ± 0.7 mm (after 25,000 cycles of progressive load increase) in the ApaPore-60 project. Although the ApaPore-60 project showed higher subsidence in the control, this was after more cycles, and the standard deviation is much lower indicating a better-controlled project. After 50,000 cycles in the BoneSave™ project one out of seven control femurs had suffered catastrophic failure. Both of the experimental groups had lower measured subsidence than the controls of allograft.

Whilst ApaPore-60 is pure hydroxyapatite (HA), BoneSave™ is a combination of 80 % Tricalcium Phosphate (TCP) and 20 % HA. TCP should resorb faster than HA which may make a difference to the long term outcomes of the two graft types, particularly if the TCP were to resorb prior to enough new bone being laid down for adequate stability. Unfortunately a direct comparison of remodelling of these synthetics was not performed for the work of this thesis.

It was noted during both of these studies that the allograft containing a synthetic behaved differently when being impacted, it did not adhere very well and had a tendency to collapse. It is possible that the cohesive properties of these synthetic bone grafts could be improved by altering their physical appearance for better interlocking. Another noted problem during impaction of the BoneSave™ / allograft mix was intra-operative fractures that had to be corrected with cerclage wiring, this may well be an effect of the stiffer nature of BoneSave™ compared to allograft. Intra-operative fractures were not observed in the Apapore-60 study, although this might be because Sawbones™ were used, cadaveric bone being more likely to have inconsistency in their strength.

As already stated the orthopaedic industry ideally needs to be striving to develop a bone graft replacement, rather than extender. Once a reliable bone graft extender has been developed it is likely that more surgeons would consider using this technique. However for a replacement to be successful it may need to "feel" a little more like allograft. Allograft has much more cohesive properties and when impacted is likely to stay where it is put, although it is likely to suffer some elastic recovery which is not necessarily beneficial. However these synthetics do not naturally adhere together when compressed although the addition of blood improves this somewhat, it does not solve this problem, so perhaps a thicker medium than blood needs to be added such as fibrin glue. This might also reduce the problem of intra-operative fractures associated with the stiffer synthetics.

The instrumentation of the slap hammer proved to be very interesting to surgeons and researchers alike. Now that a method has been created there are several avenues for further development: It could be developed as a teaching tool for surgeons new to the impaction grafting technique; instead of recording the forces, a light display could indicate the force being produced. Uncemented, off-the-shelf and custom made prostheses (CAD CAM) are used frequently for hip replacement surgery. They require specially shaped rasps to core out the femoral canal prior to a matched stem being hammered in to place. Instrumentation of such a slap hammer may give useful information as to the correct force for a firm prosthesis without fracturing the femur.

As already discussed by Grim et al (2003), the displacement per blow may give a more realistic picture of adequate impaction than the force, since for a given force the displacement per blow will reduce to virtually nothing with time. The Exeter X-change system, with the guide wire, may lend itself to this type of instrumentation. A standard way of measuring displacement is with Linear Variable differential transducers (as used in Chapter 8). These come in two parts, male and female. The male part is a thin rod, which slides inside the female part, only the female section requires a cable. It might therefore be possible to have a special guide wire made that is actually the male part, whilst the hammer could house the female part. Since the displacement per blow is the measurement before an impact minus the measurement after the impact, the capture rate could be much lower than when recording the force (200 kHz). With a lower sampling frequency it should be possible to create a program to show virtually real time results.

Another avenue for future research could be to attach strain gauges either to a cadaveric femur or Sawbone and perform impaction grafting and mechanical testing. This might highlight any aspect of impaction that was creating such stresses on the femur to cause periprosthetic fractures.

Currently clinical trials are being undertaken on BoneSave™ and ApaPore-60 by surgeons in Exeter. It would be interesting to measure the forces during these operations since some of the measurements of Chapter 4 were by a surgeon in Exeter.

9.1 Conclusions

- Currently the technique of impacting graft down the femur is highly variable between surgeons and between patients operated on by the same surgeon
- Approximately two thirds of the force generated by the surgeon is absorbed in overcoming the inertia of the hammer
- The average distal force readings range from 8.1 to 21.8 kN, which equates to 2.8 to 7.6 kN in the distal impactor
- The average proximal force readings range from 6.1 to 28.9 kN, which equates to 1.8 to 8.4 kN in the proximal impactor
- When compacted with 15 kN one hundred times Large graft (4.8 - 6.7 mm) had higher percentage porosity and lower stiffness in the axial testing to small (2.0 - 3.2 mm) and graded (0.1 - 9.4 mm) graft samples
- Following remodelling in an ovine model the bone mineral density was significantly higher at twelve weeks compared to six weeks for Small, Large and Graded graft groups
- No significant advantage in remodelling or axial stiffness could be found in using Graded graft
- The addition of 50 % BoneSave™ to allograft results in similar mechanical stiffness of 100 % allograft after six and twelve weeks remodelling in an ovine model
- When tested in Cadaveric bones addition of 50 % BoneSave™ to allograft reduces stem movement compared to a control of pure allograft
- When tested in Sawbones™ bones addition of 50 % Apapore-60 to allograft reduces stem movement compared to a control of pure allograft

Appendix 1

Load Washer Data Sheet

KISTLER

Industrielle Kraftsensoren
Capteurs de force industriels
Industrial Force Sensors

9101A ... 9104A

Kraftsensor zum Messen quasistatischer und dynamischer Kräfte für industrielle Überwachungsaufgaben.

Capteur de force pour mesurer des forces quasistatiques et dynamiques dans la surveillance industrielle.

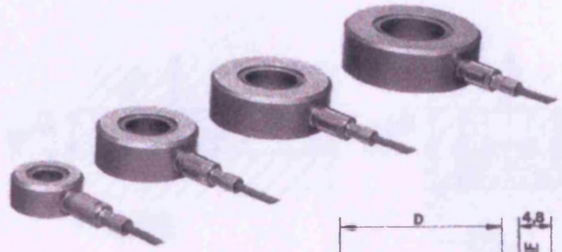
Force sensor for measuring quasistatic and dynamic forces in industrial monitoring tasks.

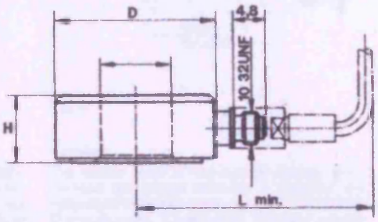
Die Kraftsensoren werden **unkalibriert** geliefert und müssen **nach** dem Einbau vor Ort kalibriert werden.

Les capteurs de force sont fournis **sans étalonnage** et doivent être étalonnés sur place **après** leur montage.

The force sensors are delivered **uncalibrated** and must be calibrated in situ **after** mounting.

- Grosser Messbereich
  Grande gamme de mesure
  Large measuring range
- Mechanisch extrem steif
  Extrêmement rigide
  Extremely rigid
- Sensor mit Kabel genügt der Schutzart IP 65
  Capteur avec câble satisfait au degré de protection IP 65
  Sensor with cable conforms to degree of protection IP 65





Type	Bereich F_z / Gamme F_z / Range F_z	Überlast / Surcharge / Overload	Max. Biegemoment M_x, M_y / Couple de flexion max. M_x, M_y / Max. bending moment M_x, M_y	Steifheit / Rigidité / Rigidity	Kapazität / Capacité / Capacitance	Gewicht / Poids / Weight	Dimensionen / Dimensions / Dimensions			
	kN	kN	Nm	kN / µm	pF	g	d (mm)	D (mm)	H (mm)	L (mm)
9101A	0 ... 20	25	15	≈1,8	23	8	6,5	14,5	8	30
9102A	0 ... 50	60	60	≈3,5	37	21	10,5	22,5	10	34
9103A	0 ... 100	120	130	≈6,0	54	38	13	28,5	11	37
9104A	0 ... 140	160	240	≈7,5	55	57	17	34,5	12	40

Allgemeine Daten	*Données générales*	*General Data*		
Empfindlichkeit	**Sensibilité**	**Sensitivity**	pC / N	≈–4,3
Linearität	**Linéarité**	**Linearity**	% FSO	<±2
Hysterese	**Hystérésis**	**Hysteresis**	% FSO	<1
Ansprechschwelle	**Seuil de réponse**	**Threshold**	N	<0.01
Isolationswiderstand	**Résistance d'isolement**	**Insulation resistance**	TΩ	>10
Temperaturkoeffizient	**Coefficient de température**	**Temperature coefficient**	% / °C	0.01
Betriebstemperaturbereich	**Gamme de température d'utilisation**	**Operating temperature range**	°C	–50 ... 120
Max. Schubkraft	**Force de cisaillement max.**	**Max. shear force**	kN	±0,1Fv*

* Fv = Vorspannung / Précontrainte / Preload

1 N = 1 kg · m · s^{-2} = 0,1019... kp = 0,2248... lbf

Anwendung

Für Überwachungsaufgaben werden Kraftsensoren gefordert, die sich problemlos in eine Maschinenstruktur einbauen lassen. Robuste Bauart und Zuverlässigkeit im Dauereinsatz sowie gute Wiederholgenauigkeit der Messwerte sind weitere Merkmale dieser Sensoren.

Gegenüber den Standard-Messunterlagscheiben Typ 9011A ... 9041A lassen sich die Kraftmessringe bei gleicher Baugrösse um 50 % höher belasten.

Die Wahl einer bestimmter Baugrösse hängt einerseits vom Einbauplatzverhältnis, andererseits vom Kraftnebenschlussverhältnis des Einbaus ab.

Application

Les problèmes de surveillance industrielle nécessitent des capteurs de force pouvant être incorporés sans problème dans une structure de machine. Une construction robuste, une fiabilité de longue durée, de même qu'une bonne fidélité des valeurs de mesure sont d'autres propriétés de ces capteurs.

Comparées aux rondelles de charge standard types 9011A ... 9041A avec les mêmes dimensions, les capteurs peuvent supporter une charge supplémentaire de 50 %.

Le choix des dimensions dépend d'une part des conditions d'installation et d'autre part des conditions de montage pour l'introduction de la force en shunt.

Application

For monitoring of industrial processes, force sensors are required, which can be easily installed in machinery. Robust design and reliability during continuous operation together with good repeatability of the measured values are additional characteristics of these sensors.

Compared to the standard load washers Types 9011A ... 9041A with identical dimensions, these sensors accept a 50 % higher load.

Selection of specific dimensions depends on the installation conditions as well as on the mounting conditions for the force shunt.

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000-108m-03.97 (D606.015m-03.97)

Anwendungsbeispiele

Überwachen von Schnittkräften an Werkzeugmaschinen, Werkzeugüberwachung in der Stanz- und Umformtechnik.

Montage

Der Sensor kann sowohl am Innen- als auch am Aussenmantel zentriert werden. Für eine Montage gemäss Fig. 2 wird die Messfläche des Sensors mit der Trennfläche der Maschinenstruktur gemeinsam überschliffen. Der Sensor darf einseitig max. je 0,20 mm abgeschliffen werden.

Je nach Anwendung wird der Sensor mit einer bestimmten Kraft verspannt. Dies geschieht durch Einlegen einer Stahlfolie (wenige µm) auf die Messfläche des Sensors (Fig. 2) oder durch Vorspannen mit einer Spezialmutter (Fig. 1 und 3).

Exemples d'application

Surveillance des efforts de coupe sur machines-outils, surveillance de l'outil utilisé pour l'estampage et le formage.

Montage

Le capteur peut être centré à l'aide de sa surface latérale intérieure ou extérieure. Si le montage est effectué comme indiqué dans fig. 2, la surface de mesure du capteur doit être rectifiée ensemble avec le niveau de séparation de la structure. Le capteur peut être rectifié de 0,20 mm max. d'un côté.

Dépendant de l'application, le capteur est précontraint avec une force déterminée. Ceci est réalisé par l'insertion d'une feuille d'acier (quelques µm) sur la surface de mesure du capteur (fig. 2) ou par la précontrainte à l'aide d'un écrou spécial (fig. 1 et 3).

Application Examples

Monitoring of cutting forces on machine-tools, tool monitoring of punching and metal forming machines.

Mounting

The outer or inner casing can be used to center the sensor. If the mounting is effected according to Fig. 2, the measuring surface of the sensor must be ground together with the separation level of the structure. Grounding can be done up to max. 0,20 mm depth on one side of the sensor.

Depending on application, the sensor is preloaded with a specific preloading force. This is done by inserting a steel foil (several µm thick) on the measuring surface of the sensor (Fig. 2), or by preloading by means of a special nut (Fig. 1 and 3).

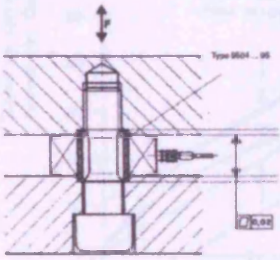

Fig. 1

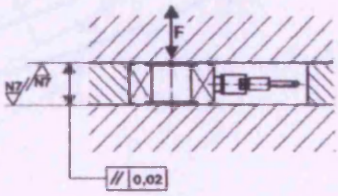

Fig. 2

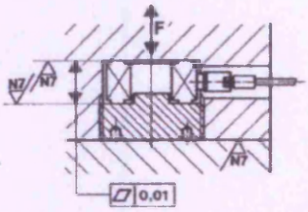

Fig. 3

Kabelkonzept

Der Sensorkörper ist hermetisch dicht. Bei erhöhten Anforderungen an die Betriebssicherheit wird der industrietauglich integrierte Kabelstecker UNF 10-32 mit O-Ring eingesetzt. Bei Bedarf kann der Stecker mit dem Sensorgehäuse dicht verschweisst werden. Das Kabel ist mit Vorteil ohne zusätzliches Verlängerungskabel direkt in ein dichtes Gehäuse (Verteilkasten, Ladungsverstärker) zu führen.

Câblage

Le corps du capteur est étanche. Si une fiabilité encore plus grande est exigée, le connecteur à câble intégré industriel UNF 10-32 est utilisé avec un joint torique. Si nécessaire, le connecteur peut être soudé étanche avec le boîtier. Il est avantageux d'amener le câble directement dans un boîtier étanche (boîte de distribution, amplificateur de charge) sans utiliser un câble de rallonge.

Cabling

The sensor case is hermetically sealed. If increased operational reliability is required, the integrated industrial cable plug UNF 10-32 with O-ring is used. If necessary, the plug can be welded leakproof to the sensor casing. It is advantageous to lead the cable without any additional extension cable directly into a leakproof housing (distribution box, charge amplifier).

Kabelstecker UNF 10-32 integriert, mit O-Ring gedichtet oder geschweisst.

Connecteur à câble UNF 10-32 intégré, étanchéifié avec joint torique ou soudé.

Cable plug UNF 10-32 integrated, sealed with O-ring or soldered.

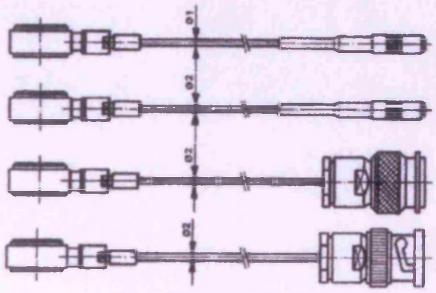

Fig. 4: Anschlusskabel-Varianten / Variantes pour câbles de connexion / Variants for connecting cables

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Das Anschlusskabel ist nicht im Lieferumfang enthalten und kann separat bestellt werden.

Le câble de connexion ne fait pas partie de la livraison; il peut être commandé séparément.

The connecting cable is not included in the delivery; it can be ordered separately.

Elektronik

Für industrielle Überwachungsaufgaben wird mit Vorteil der Ladungsverstärker in der Nähe des Sensors montiert. Für diesen Einsatz eignen sich industrielle Ladungsverstärker in dichtem Gehäuse.

Electronique

Pour des tâches de surveillance industrielles l'amplificateur de charge est installé de préférence dans le voisinage du capteur. Pour cette application, des amplificateurs de charge industriels dans boîtiers étanches sont utilisés.

Electronics

For industrial monitoring tasks the charge amplifier is advantageously installed in the vicinity of the sensor. For this application industrial charge amplifiers in leakproof housings are used.

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Linearity (ISA): The closeness of a calibration curve to a specified straight line.

For piezoelectric force transducers this straight line is determined as follows (see Fig. 4; to make matters clearer the curve has been distorted in the ordinate direction):

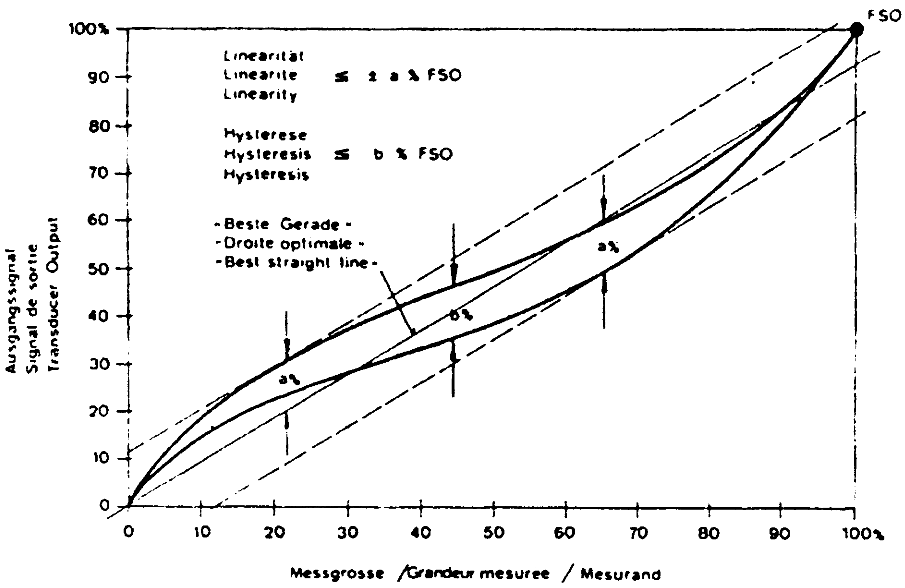

Figure R1 – Calibration curve of Load washer showing hysteresis

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